NOVEL PROTEINS AND NUCLEIC ACIDS ENCODING SAME

RELATED APPLICATIONS

This application claims priority from USSN 60/186,592, filed March 3, 2000; USSN 60/186,718, filed March 3, 2000; USSN 60/187,293, filed March 6, 2000; USSN 60/187,294, filed March 6, 2000; USSN 60/190,400, filed March 17, 2000; ; USSN 60/196,018, filed April 7, 2000; USSN 60/259,548, filed January 3, 2001; each of which is incorporated by reference in its entirety.

BACKGROUND OF THE INVENTION

The invention relates generally to polynucleotides and polypeptides, as well as vectors, host cells, antibodies, and recombinant methods for producing these nucleic acids and polypeptides.

SUMMARY OF THE INVENTION

The invention is based in part upon the discovery of novel nucleic acid sequences encoding novel polypeptides. The disclosed FCTR1, FCTR2, FCTR3, FCTR4, FCTR5, FCTR6 and FCTR7 nucleic acids and polypeptides encoded therefrom, as well as derivatives, homologs, analogs and fragments thereof, will hereinafter be collectively designated as "FCTRX" nucleic acid or polypeptide sequences.

In one aspect, the invention provides an isolated FCTRX nucleic acid molecule encoding a FCTRX polypeptide that includes a nucleic acid sequence that has identity to the nucleic acids disclosed in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24. In some embodiments, the FCTRX nucleic acid molecule will hybridize under stringent conditions to a nucleic acid sequence complementary to a nucleic acid molecule that includes a protein-coding sequence of a FCTRX nucleic acid sequence. The invention also includes an isolated nucleic acid that encodes a FCTRX polypeptide, or a fragment, homolog, analog or derivative thereof. For example, the nucleic acid can encode a polypeptide at least 80% identical to a polypeptide comprising the amino acid sequences of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. The nucleic acid can be, for example, a genomic DNA fragment or a cDNA molecule that

includes the nucleic acid sequence of any of SEQ ID NOS: 1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24.

Also included in the invention is an oligonucleotide, *e.g.*, an oligonucleotide which includes at least 6 contiguous nucleotides of a FCTRX nucleic acid (*e.g.*, SEQ ID NOS: 1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24) or a complement of said oligonucleotide.

Also included in the invention are substantially purified FCTRX polypeptides (SEQ ID NO: 2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25). In certain embodiments, the FCTRX polypeptides include an amino acid sequence that is substantially identical to the amino acid sequence of a human FCTRX polypeptide.

The invention also features antibodies that immunoselectively-binds to FCTRX polypeptides, or fragments, homologs, analogs or derivatives thereof.

In another aspect, the invention includes pharmaceutical compositions that include therapeutically- or prophylactically-effective amounts of a therapeutic and a pharmaceutically-acceptable carrier. The therapeutic can be, *e.g.*, a FCTRX nucleic acid, a FCTRX polypeptide, or an antibody specific for a FCTRX polypeptide. In a further aspect, the invention includes, in one or more containers, a therapeutically- or prophylactically-effective amount of this pharmaceutical composition.

In a further aspect, the invention includes a method of producing a polypeptide by culturing a cell that includes a FCTRX nucleic acid, under conditions allowing for expression of the FCTRX polypeptide encoded by the DNA. If desired, the FCTRX polypeptide can then be recovered.

In another aspect, the invention includes a method of detecting the presence of a FCTRX polypeptide in a sample. In the method, a sample is contacted with a compound that selectively binds to the polypeptide under conditions allowing for formation of a complex between the polypeptide and the compound. The complex is detected, if present, thereby identifying the FCTRX polypeptide within the sample.

The invention also includes methods to identify specific cell or tissue types based on their expression of a FCTRX.

Also included in the invention is a method of detecting the presence of a FCTRX nucleic acid molecule in a sample by contacting the sample with a FCTRX nucleic acid probe or primer, and detecting whether the nucleic acid probe or primer bound to a FCTRX nucleic acid molecule in the sample.

In a further aspect, the invention provides a method for modulating the activity of a FCTRX polypeptide by contacting a cell sample that includes the FCTRX polypeptide with a

compound that binds to the FCTRX polypeptide in an amount sufficient to modulate the activity of said polypeptide. The compound can be, *e.g.*, a small molecule, such as a nucleic acid, peptide, polypeptide, peptidomimetic, carbohydrate, lipid or other organic (carbon containing) or inorganic molecule, as further described herein.

Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital ceonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma , clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveilance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy. The Therapeutic can be, *e.g.*, a FCTRX nucleic acid, a FCTRX polypeptide, or a FCTRX-specific antibody, or biologically-active derivatives or fragments thereof.

The invention further includes a method for screening for a modulator of disorders or syndromes including, *e.g.*, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital ceonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast

adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveilance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy. The method includes contacting a test compound with a FCTRX polypeptide and determining if the test compound binds to said FCTRX polypeptide. Binding of the test compound to the FCTRX polypeptide indicates the test compound is a modulator of activity, or of latency or predisposition to the aforementioned disorders or syndromes.

Also within the scope of the invention is a method for screening for a modulator of activity, or of latency or predisposition to an disorders or syndromes including, *e.g.*, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital ceonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma , clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveilance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy,

demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy by administering a test compound to a test animal at increased risk for the aforementioned disorders or syndromes. The test animal expresses a recombinant polypeptide encoded by a FCTRX nucleic acid. Expression or activity of FCTRX polypeptide is then measured in the test animal, as is expression or activity of the protein in a control animal which recombinantly-expresses FCTRX polypeptide and is not at increased risk for the disorder or syndrome. Next, the expression of FCTRX polypeptide in both the test animal and the control animal is compared. A change in the activity of FCTRX polypeptide in the test animal relative to the control animal indicates the test compound is a modulator of latency of the disorder or syndrome.

In yet another aspect, the invention includes a method for determining the presence of or predisposition to a disease associated with altered levels of a FCTRX polypeptide, a FCTRX nucleic acid, or both, in a subject (*e.g.*, a human subject). The method includes measuring the amount of the FCTRX polypeptide in a test sample from the subject and comparing the amount of the polypeptide in the test sample to the amount of the FCTRX polypeptide present in a control sample. An alteration in the level of the FCTRX polypeptide in the test sample as compared to the control sample indicates the presence of or predisposition to a disease in the subject. Preferably, the predisposition includes, *e.g.*, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital ceonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma , clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell

mediated immune effector cells and pathways resulting in tumor escape from immune surveilance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy. Also, the expression levels of the new polypeptides of the invention can be used in a method to screen for various cancers as well as to determine the stage of cancers.

In a further aspect, the invention includes a method of treating or preventing a pathological condition associated with a disorder in a mammal by administering to the subject a FCTRX polypeptide, a FCTRX nucleic acid, or a FCTRX-specific antibody to a subject (*e.g.*, a human subject), in an amount sufficient to alleviate or prevent the pathological condition. In preferred embodiments, the disorder, includes, *e.g.*, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital ceonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma , clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveilance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome,

liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spino[redacted]ebellar ataxia, Plasmodium falciparum[redacted]arasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy.

In yet another aspect, the invention can be used in a method to identity the cellular receptors and downstream effectors of the invention by any one of a number of techniques commonly employed in the art. These include but are not limited to the two-hybrid system, affinity purification, co-precipitation with antibodies or other specific-interacting molecules.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In the case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

Other features and advantages of the invention will be apparent from the following detailed description and claims.

DETAILED DESCRIPTION

The invention is based, in part, upon the discovery of novel nucleic acid sequences that encode novel polypeptides. The novel nucleic acids and their encoded polypeptides are referred to individually as FCTR1, FCTR2, FCTR3, FCTR4, FCTR5, FCTR6, and FCTR7. The nucleic acids, and their encoded polypeptides, are collectively designated herein as "FCTRX".

The novel FCTRX nucleic acids of the invention include the nucleic acids whose sequences are provided in Tables 1A, 2A, 3A, 3C, 3E, 3F, 3G, 3H, 4A, 5A, 5C, 5E, 6A, 6C, and 7A inclusive ("Tables 1A - 7A"), or a fragment, derivative, analog or homolog thereof. The novel FCTRX proteins of the invention include the protein fragments whose sequences are provided in Tables 1B, 2B, 3B, 3I, 4B, 5B, 5D, 6B, 6D, and 7B inclusive ("Tables 1B - 7B"). The individual FCTRX nucleic acids and proteins are described below. Within the scope of this invention is a method of using these nucleic acids and peptides in the treatment or prevention of a disorder related to cell signaling or metabolic pathway modulation.

FCTR1

Novel FCTR1 is a growth factor ("FCTR") protein related to follistatin-like gene, and mac25. FCTR1 (also referred to by proprietary accession number 58092213.0.36) is a full-length clone of 771 nucleotides, including the entire coding sequence of a 105 amino acid protein from nucleotides 438 to 753. The clone was originally obtained from thyroid gland, kidney, fetal kidney, and spleen tissues.

The nucleotide sequence of FCTR1 as presently determined is reported in Table 1A. The start and stop codons are bolded and the 5' and 3' untranslated regions are underlined.

Table 1A. FCTR1 nucleotide sequence (SEQ ID NO:1).

GGTCCTCACCCCCTTCCTCTCTCCCAGCCTCGGTGTCTGGTTACGGCTCCTCTGCTCGCATTGTGACTTTGGGCCAGGCTGGGGGA
AATGACCCGGGAGGGTCCCATGCGGCTACATAAAATTGGCAGCCTTAGAACTAGTGGGAAGGCGGGTGCGCGAAGTCGAGGGGCGG
AGAGAGGGGGCCGGAGGAGCTGCTTTCTGAATCCAAGTTCGTGGGCTCTCTCAGAAGTCCTCAGGACGGAGCAGAGGTGGCCGGCG
GGCCCGGCTGACTGCGCCTCTGCTTTCTTTCCATAACCTTTTCTTTCGGACTCGAATCACGGCTGCTGCGAAGGGTCTAGTTCCGG
ACACTAGGGCCCCAGATCGTGTCACATCCATATGACACTTGGAATGTGACAGGGCAGGATGTGATCTTTGGCTGTGAAGTGTTTGC
CTACCCC**ATG**GCCTCCATCGAGTGGAGGAAGGATGGCTTGGACATCCAGCTGCCAGGGGATGACCCCCACATCTCTGTGCAGTTTA
GGGGTGGACCCCAGAGGTTTGAGGTGACTGGCTGGCTGCAGATCCAGGCTGTGCGTCCCAGTGATGAGGGCACTTACCGCTGCCTT
GCCCGCAATGCCCTGGGTCAAGTGGAGGCCCCTGCTAGCTTGACAGTGCTCACACCTGACCAGCTGAACTCTACAGGCATCCCCCA
GCTGCGATCACTAAACCTGGTTCCTGAGGAGGAGGCTGAGAGTGAAGAGAATGACGATTACTAC**TAG**GTCCAGAGCTCTGGCC

The predicted amino acid sequence of FCTR1 protein corresponding to the foregoing nucleotide sequence is reported in Table 1B. FCTR1 was searched against other databases using SignalPep and PSort search protocols. The protein is most likely located in the cytoplasm (certainty=0.6500) and seems to have no N-terminal signal sequence. The predicted molecular weight of FCTR1 protein is 11711.8 daltons.

Table 1B. Encoded FCTR1 protein sequence (SEQ ID NO:2).

MASIEWRKDGLDIQLPGDDPHISVQFRGGPQRFEVTGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVLTPDQLNSTGIPQLR
SLNLVPEEEAESEENDDYY

FCTR1 was initially identified with a TblastN analysis of a proprietary sequence file for a follistatin-like probe or homolog which was run against the Genomic Daily Files made available by GenBank. A proprietary software program (GenScan™) was used to further predict the nucleic acid sequence and the selection of exons. The resulting sequences were further modified by means of similarities using BLAST searches. The sequences were then manually corrected for apparent inconsistencies, thereby obtaining the sequences encoding the full-length protein.

In an analysis of sequence databases, it was found, for example, that the FCTR1 nucleic acid sequence has 31/71 bases (43%) identical and 46/71 bases positively alike to a *Mus Musculus* IGFBP-like protein (TREMBL Accession Number:BAA21725) shown in Table 1C. In all BLAST alignments herein, the "E-value" or "Expect" value is a numeric indication of the probability that the aligned sequences could have achieved their similarity to the BLAST query

sequence by chance alone within the database that was searched. For example, as shown in Table 1C, the probability that the subject ("Sbjct") retrieved from the FCTR1 BLAST analysis, in this case the *Mus Musculus* IGFBP-like protein, matched the Query FCTR1 sequence purely by chance is $1.2x10^{-11}$.

Table 1C. BLASTP of FCTR1 against *Mus Musculus* IGFBP-like protein (SEQ ID NO:38)

```
PTNR:REMTREMBL-ACC:BAA21725 IGFBP-LIKE PROTEIN - MUS MUSCULUS (MOUSE), 270 AA.
LENGTH = 270

 SCORE = 161 (56.7 BITS), EXPECT = 1.2E-11, P = 1.2E-11
 IDENTITIES = 31/71 (43%), POSITIVES = 46/71 (64%)

QUERY:      9 DGLDIQLPGDDPHISVQFRGGPQRFEVTGWLQIQAVRPSDEGTYRCLARNALGQVEAPAS 68
              +||+ +|||| +|+|| |||| | | |+ | +| ||| | | | ||+|+ ++ +
SBJCT:    191 EGLE-ELPGDHVNIAVQVRGGPSDHETTSWILINPLRKEDEGVYHCHAANAIGEAQSHGT 249

QUERY:     69 LTVLTPDQLNS 79
              +|||  ++  |
SBJCT:    250 VTVLDLNRYKS 260
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The amino acid sequence of FCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Mus Musculus* Follistatin-like Protein shown in Table 1D.

Table 1D. BLASTP of FCTR1 against *Mus Musculus* Follistatin-like Protein (SEQ ID NO:39)

```
PTNR:SPTREMBL-ACC:Q61581 FOLLISTATIN-LIKE 2 (FOLLISTATIN-LIKE PROTEIN) - MUS MUSCULUS
(MOUSE), 238 AA.
            LENGTH = 238

 SCORE = 149 (52.5 BITS), EXPECT = 1.5E-10, P = 1.5E-10
 IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)

QUERY:     15 LPGDDPHISVQFRGGPQRFEVTGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVL 72
              ||||  ++++|_||||++ |||||+ +  +   | | | | | |+ ||  | | +||+
SBJCT:    165 LPGDRENLAIQTRGGPEKHEVTGWVLVSPLSKEDAGEYECHASNSQGQASAAAKITVV 222
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The amino acid sequence of FCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Homo sapiens* MAC25 protein shown in Table 1E.

Table 1E. BLASTP of FCTR1 against *Homo sapiens* MAC25 protein (SEQ ID NO:40)

```
PTNR:SPTREMBL-ACC:Q07822 MAC25 PROTEIN - HOMO SAPIENS (HUMAN), 277 AA.
            LENGTH = 277

 SCORE = 149 (52.5 BITS), EXPECT = 3.2E-10, P = 3.2E-10
 IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)

QUERY:     15 LPGDDPHISVQFRGGPQRFEVTGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVL 72
              ||||  ++++| |||||++ |||||+ +  +   | | | | | |+ ||  | | +||+
SBJCT:    209 LPGDRDNLAIQTRGGPEKHEVTGWVLVSPLSKEDAGEYECHASNSQGQASASAKITVV 266
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The amino acid sequence of FCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Mus musculus* MAC25 protein shown in Table 1F.

Table 1F. BLASTP of FCTR1 against *Mus musculus* MAC25 protein (SEQ ID NO:41)

```
PTNR:SPTREMBL-ACC:O88812 MAC25 - MUS MUSCULUS (MOUSE), 281 AA
            LENGTH = 281

 SCORE = 149 (52.5 BITS), EXPECT = 3.4E-10, P = 3.4E-10
 IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)

QUERY:    15 LPGDDPHISVQFRGGPQRFEVTGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVL 72
             ||||  ++++| ||||++ |||||+ +  +   | | | | | |+ ||  | | +||+
SBJCT:   208 LPGDRENLAIQTRGGPEKHEVTGWVLVSPLSKEDAGEYECHASNSQGQASAAAKITVV 265
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The amino acid sequence of FCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Homo sapiens* Prostacyclin-stimulating factor shown in Table 1G.

Table 1G. BLASTP of FCTR1 against *Homo sapiens* Prostacyclin-stimulating factor (SEQ ID NO:42)

```
PTNR:SPTREMBL-ACC:Q16270 PROSTACYCLIN-STIMULATING FACTOR - HOMO SAPIENS (HUMAN), 282
AA
            LENGTH = 282

 SCORE = 149 (52.5 BITS), EXPECT = 3.4E-10, P = 3.4E-10
 IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)

QUERY:    15 LPGDDPHISVQFRGGPQRFEVTGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVL 72
             ||||  ++++| ||||++ |||||+ +  +   | | | | | |+ ||  | | +||+
SBJCT:   209 LPGDRDNLAIQTRGGPEKHEVTGWVLVSPLSKEDAGEYECHASNSQGQASASAKITVV 266
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The amino acid sequence of FCTR1 also had 18/44 bases (40%) identical, and 25/44 bases (56%) positive for rat Colorectal cancer suppressor shown in Table 1H.

Table 1H. BLASTP of FCTR1 against rat Colorectal cancer suppressor (SEQ ID NO:43)

```
PTNR:PIR-ID:B40098 COLORECTAL CANCER SUPPRESSOR DCC - RAT (FRAGMENTS)
            LENGTH = 144

 SCORE = 78 (27.5 BITS), EXPECT = 1.1E-05, SUM P(2) = 1.1E-05
 IDENTITIES = 18/44 (40%), POSITIVES = 25/44 (56%)

QUERY:    33 FEVTGW--LQIQAVRPSDEGTYRCLARNALGQVEAPASLTVLTP 74
             |++ |   |+|  |  |||| |+|+| |  |  ++ | | |  |
SBJCT:   101 FQIVGGSNLRILGVVKSDEGFYQCVAENEAGNAQSSAQLIVPKP 144

 SCORE = 37 (13.0 BITS), EXPECT = 1.1E-05, SUM P(2) = 1.1E-05
 IDENTITIES = 8/19 (42%), POSITIVES = 12/19 (63%)

QUERY:     1 MASIEWRKDGLDIQL-PGD 18
             | +| |+|+  |+   |||
SBJCT:    30 MPTIHWQKNQQDLTPNPGD 48
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The amino acid sequence of FCTR1 also had 32/83 bases (38%) identical, and 45/83 bases (54%) positive to bases 55-137, and 24/68 bases (35%) identical, and 37/68 bases (54%) positive to bases 166-225 of *Homo sapiens* PTPsigma-(Brain) Precursor shown in Table 1I.

Table 1I. BLASTP of FCTR1 against *Homo sapiens* PTPsigma-(Brain) Precursor (SEQ ID NO:44)

```
PTNR:TREMBLNEW-ACC:AAD09360 PTPSIGMA-(BRAIN) PRECURSOR - HOMO SAPIENS (HUMAN), 1502
AA.
            LENGTH = 1502

 SCORE = 109 (38.4 BITS), EXPECT = 0.00010, P = 0.00010
 IDENTITIES = 32/83 (38%), POSITIVES = 45/83 (54%)

QUERY:    14 QLPGDD-PHISVQFRG---GPQRFEVTGW-------LQIQAVR-PSDEGTYRCLARNALG 61
             |  ||  | ++   +|     ||||   +       |+|| +| | ||  | |+|+|++|
SBJCT:    55 QATGDPKPRVTWNKKGKKVNSQRFETIEFDESAGAVLRIQPLRTPRDENVYECVAQNSVG 114

QUERY:    62 QVEAPASLTVLTPDQLNSTGIPQL 85
             ++   | ||||  ||| | | | +
SBJCT:   115 EITVHAKLTVLREDQLPS-GFPNI 137

 SCORE = 77 (27.1 BITS), EXPECT = 0.25, P = 0.22
 IDENTITIES = 24/68 (35%), POSITIVES = 37/68 (54%)

QUERY:     4 IEWRKDGLDIQLPGDDPHISVQFRGGPQRFEVTGWLQIQAVRPSDEGTYRCLARNALG-Q 62
             | | || | +     ||  |    | ++   +| |||++   +|+| | |+| |+ | +
SBJCT:   166 ITWFKDFLPV-----DPSAS---NGRIKQLR-SGALQIESSEETDQGKYECVATNSAGVR 216

QUERY:    63 VEAPASLTV 71
               +||+| |
SBJCT:   217 YSSPANLYV 225
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The amino acid sequence of FCTR1 also had 32/83 bases (38%) identical, and 45/83 bases (54%) positive for amino acids 55-137 and 26/69 bases (37%) identical, and 38/69 (54%) positive for amino acids 166-234 of *Homo sapiens* Protein-Tyrosine Phosphatase Sigma shown in Table 1J.

Table 1J. BLASTP of FCTR1 against *Homo sapiens* PTPsigma-(Brain) Precursor (SEQ ID NO:45)

```
PTNR:SPTREMBL-ACC:Q13332 PROTEIN-TYROSINE PHOSPHATASE, RECEPTOR-TYPE, S PRECURSOR (EC
3.1.3.48) (PROTEIN-TYROSINE PHOSPHATASE SIGMA) (R-PTP-SIGMA) (PTPRS) - HOMO SAPIENS
(HUMAN), 1948 AA.
LENGTH = 1948

 SCORE = 109 (38.4 BITS), EXPECT = 0.00013, P = 0.00013
 IDENTITIES = 32/83 (38%), POSITIVES = 45/83 (54%)

QUERY:    14 QLPGDD-PHISVQFRG---GPQRFEVTGW-------LQIQAVR-PSDEGTYRCLARNALG 61
             |  ||  | ++   +|     ||||   +       |+|| +| | ||  | |+|+|++|
SBJCT:    55 QATGDPKPRVTWNKKGKKVNSQRFETIEFDESAGAVLRIQPLRTPRDENVYECVAQNSVG 114

QUERY:    62 QVEAPASLTVLTPDQLNSTGIPQL 85
             ++   | ||||  ||| | | | +
SBJCT:   115 EITVHAKLTVLREDQLPS-GFPNI 137

 SCORE = 88 (31.0 BITS), EXPECT = 0.023, P = 0.022
 IDENTITIES = 26/69 (37%), POSITIVES = 38/69 (55%)
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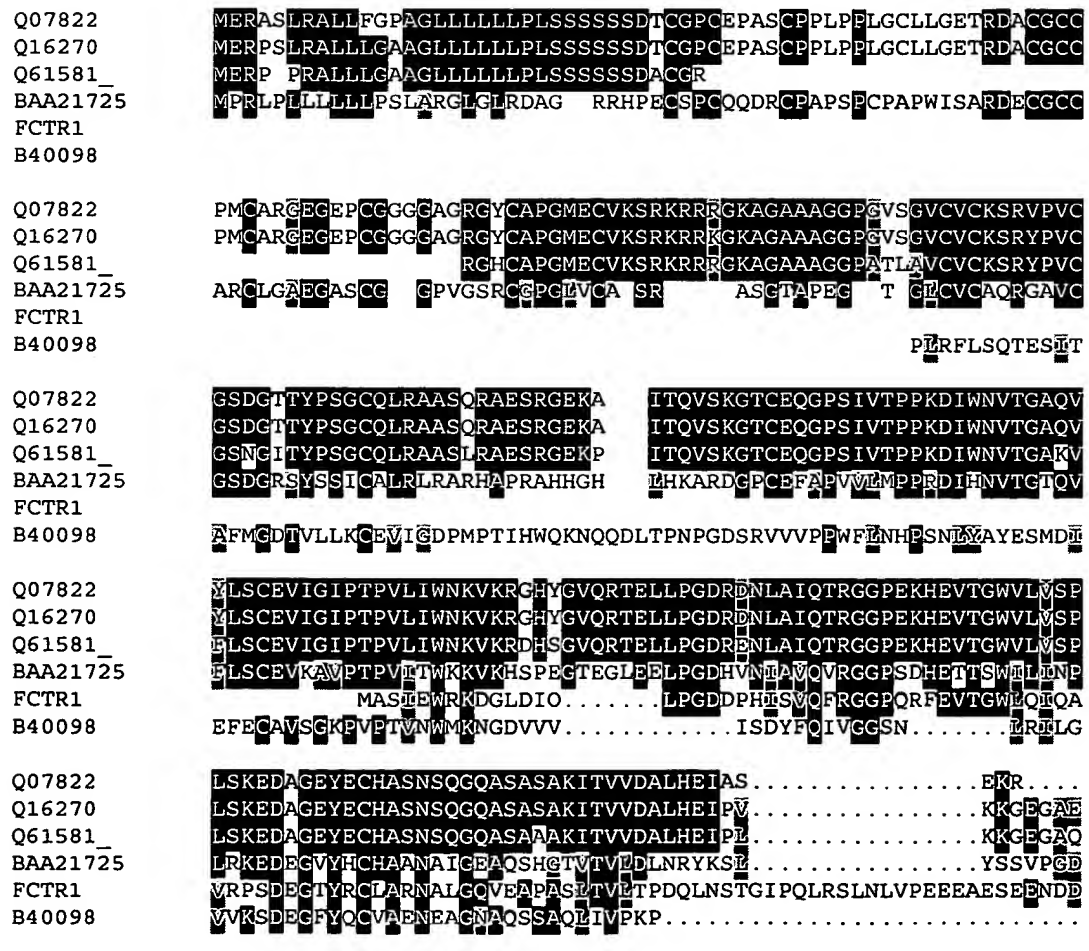
QUERY:      4 IEWRKDGLDIQLPGDDPHISVQFRGGPQRFEVT---GWLQIQAVRPSDEGTYRCLARNAL 60
              | | || |[redacted]     +  |  | |   + || |   | |||++ [redacted]| | |+| |+
SBJCT:    166 ITWFKDFL[redacted]SASNGRIK-QLRS--ETFESTPIRGALQIESSE[redacted]QGKYECVATNSA 222

QUERY:     61 G-QVEAPASLTV 71
              | +  +||+| |
SBJCT:    223 GVRYSSPANLYV 234
```

A ClustalW analysis comparing the protein of the invention with related protein sequences is given in Table 1K, with FCTR1 shown on line 2. In the ClustalW alignment of the FCTR1 protein, as well as all other ClustalW analyses herein, the black outlined amino acid residues indicate regions of conserved sequence (*i.e.*, regions that may be required to preserve structural or functional properties), whereas non-highlighted amino acid residues are less conserved and can potentially be mutated to a much broader extent without altering protein structure or function.

Table 1K. ClustalW Analysis of FCTR1

1) Q07822 MAC25 PROTEIN. (SEQ ID NO:40)
2) Q16270 PROSTACYCLIN-STIMULATING FACTOR. (SEQ ID NO:42)
3) Q61581_FOLLISTATIN-LIKE 2: FOLLISTATIN-LIKE 2 (FOLLISTATIN-LIKE PROTEIN) (SEQ ID NO:39)
4) BAA21725 IGFBP-LIKE PROTEIN (SEQ ID NO:38)
5) FCTR1 (SEQ ID NO:2)
6) B40098 COLORECTAL CANCER SUPPRESSOR DCC - RAT (FRAGMENTS) (SEQ ID NO:43)



Q07822
Q16270 [redacted].
Q61581_ [redacted].
BAA21725 [redacted]L
FCTR1 YY

IGFBP is expressed in neurostem cell and developing central nervous system. MAC-25, a follistatin like protein is a growth suppressor of osteosarcoma cells, and meningiomas. DCC is expressed in most normal tissues especially in colonic mucosa, but is deleted in colorectal cancers.

Since FCTR1 has similarity to these proteins (shown in BlastP, Tables 1C-1J, and in clustalW, Table 1K) it is likely that it has similar function. Therefore FCTR1 could function as on or more of the following: a tumor suppressor geneor regulator of neurological system development.

Based on the protein similarity and tissue expression, FCTR1 may be useful in the following diseases and uses:

(i) Tissue regeneration in vitro and in vivo

(ii) Neurological disorders, neurodegenerative disorders, nerve trauma

(iii) Reproductive health

(iv) Immunological disorders, allergy and infection

(v) In cancer as a diagnostic and prognostic marker, as well as a protein therapeutic

FCTR2

FCTR2 (alternatively referred to herein as AC012614_1.0.123), is a growth factor bearing sequence similarity to human KIAA1061 protein and to genes involved in neuronal development and reproductive physiology (e.g., cell adhesion molecules, follistatin, roundabout and frazzled). FCTR2 is a full-length clone of 5502 nucleotides, including the entire coding sequence of a 815 amino acid protein. This sequence is expressed in glioma, osteoblast, other cancer cells, lung carcinoma, small intestine (This sequence maps to Unigene Hs.123420 which is expressed in brain, breast, kidney, pancreas, pooled tissue).

A FCTR2 ORF begins with an ATG initiation codon at nucleotides 420-422 and ends with a TGA codon at nucleotides 2865-2867. Putative untranslated regions upstream from the initiation codon and downstream from the termination codon are underlined in Table 2A, and the start and stop codons are in bold letters.

Table 2A. FCTR2 Nucleotide Sequence (SEQ ID NO:3).

CAATTTCACACAGGAAACAGCTATGCCATGATTACGCAAGTTGGTACCGAGCTCGGATCCACTAGTAACGGCCGCCAGTG
TGCTGGAATTCGGCTTACTCACTATAGGGCTCGAGCGGCTGCCCGGGCAGGTCATTAATTCCATTTCTTTTTAGAGTATC
ACAGCTTTCTCCTTCACTGACCACCCTTTGCTTCCTGTCAGAAAGCCCTGGACAGAACTCTCTGTGGGATTCTGCCCATG

TTTCTGAGATATCGCCTCAATTGTCCTGGCTGGGCTGTCGGGTCTGCCCGTTTTACAGATGGGCAAACTGGAGTGGGAAG
TATCCGGGTGGCTTCCTCAGG[redacted]CAGCTGGTGGAGCAGCTACTGAAACAATCAGG[redacted]CAGAAGCTTTGAAGTCACA
AGAAGAGAAGACTCCCAGAAT[redacted]TGTGATGTTGGTGATGGACGCCTGTTTCGCCTT[redacted]CTTAAACGTGCCCTTTCCA
GCTGCCCTGACCTCTTTGGGCTTTCCAGCCGCAACGAGCTGCTGGCCTCCTGCGGGAAGAAGTTCTGCAGCCGAGGGAGC
CGGTGCGTGCTCAGCAGGAAGACAGGGGAGCCCGAATGCCAGTGCCTGGAGGCATGCAGGCCCAGCTACGTGCCTGTGTG
CGGCTCTGATGGGAGGTTTTATGAAAACCACTGTAAGCTCCACCGTGCTGCTTGCCTCCTGGGAAAGAGGATCACCGTCA
TCCACAGCAAGGACTGTTTCCTCAAAGGTGACACGTGCACCATGGCCGGCTACGCCCGCTTGAAGAATGTCCTTCTGGCA
CTCCAGACCCGTCTGCAGCCACTCCAAGAAGGAGACAGCAGACAAGACCCTGCCTCCCAGAAGCGCCTCCTGGTGGAATC
TCTGTTCAGGGACTTAGATGCAGATGGCAATGGCCACCTCAGCAGCTCCGAACTGGCTCAGCATGTGCTGAAGAAGCAGG
ACCTGGATGAAGACTTACTTGGTTGCTCACCAGGTGACCTCCTCCGATTTGACGATTACAACAGTGACAGCTCCCTGACC
CTCCGCGAGTTCTACATGGCCTTCCAAGTGGTTCAGCTCAGCCTCGCCCCCGAGGACAGGGTCAGTGTGACCACAGTGAC
CGTGGGGCTGAGCACAGTGCTGACCTGCGCCGTCCATGGAGACCTGAGGCCACCAATCATCTGGAAGCGCAACGGGCTCA
CCCTGAACTTCCTGGACTTGGAAGACATCAATGACTTTGGAGAGGATGATTCCCTGTACATCACCAAGGTGACCACCATC
CACATGGGCAATTACACCTGCCATGCTTCCGGCCACGAGCAGCTGTTCCAGACCCACGTCCTGCAGGTGAATGTGCCGCC
AGTCATCCGTGTCTATCCAGAGAGCCAGGCACAGGAGCCTGGAGTGGCAGCCAGCCTAAGATGCCATGCTGAGGGCATTC
CCATGCCCAGAATCACTTGGCTGAAAAACGGCGTGGATGTCTCAACTCAGATGTCCAAACAGCTCTCCCTTTTAGCCAAT
GGGAGCGAACTCCACATCAGCAGTGTTCGGTATGAAGACACAGGGGCATACACCTGCATTGCCAAAAATGAAGTGGGTGT
GGATGAAGATATCTCCTCGCTCTTCATTGAAGACTCAGCTAGAAAGACCCTTGCAAACATCCTGTGGCGAGAGGAAGGCC
TCAGCGTGGGAAACATGTTCTATGTCTTCTCCGACGACGGTATCATCGTCATCCATCCTGTGGACTGTGAGATCCAGAGG
CACCTCAAACCCACGGAAAAGATTTTCATGAGCTATGAAGAAATCTGTCCTCAAAGAGAAAAAAATGCAACCCAGCCCTG
CCAGTGGGTATCTGCAGTCAATGTCCGGAACCGGTACATCTATGTGGCCCAGCCAGCACTGAGCAGAGTCCTTGTGGTCG
ACATCCAAGCCCAGAAAGTCCTACAGTCCATAGGTGTGGACCCTCTGCCGGCTAAGCTGTCCTATGACAAGTCACATGAC
CAAGTGTGGGTCCTGAGCTGGGGGGACGTGCACAAGTCCCGACCAAGTCTCCAGGTGATCACAGAAGCCAGCACCGGCCA
GAGCCAGCACCTCATCCGCACACCCTTTGCAGGAGTGGATGATTTCTTCATTCCCCCAACAAACCTCATCATCAACCACA
TCAGGTTTGGCTTCATCTTCAACAAGTCTGATCCTGCAGTCCACAAGGTGGACCTGGAAACAATGATGCCCCTCAAGACC
ATCGGCCTGCACCACCATGGCTGCGTGCCCCAGGCCATGGCACACACCCACCTGGGCGGCTACTTCTTCATCCAGTGCCG
ACAGGACAGCCCCGCCTCTGCTGCCCGACAGCTGCTCGTTGACAGTGTCACAGACTCTGTGCTTGGCCCCAATGGTGATG
TAACAGGCACCCCACACACATCCCCCGACGGGCGCTTCATAGTCAGTGCTGCAGCTGACAGCCCCTGGCTGCACGTGCAG
GAGATCACAGTGCGGGGCGAGATCCAGACCCTGTATGACCTGCAAATAAACTCGGGCATCTCAGACTTGGCCTTCCAGCG
CTCCTTCACTGAAAGCAATCAATACAACATCTACGCGGCTCTGCACACGGAGCCGGACCTGCTGTTCCTGGAGCTGTCCA
CGGGGAAGGTGGGCATGCTGAAGAACTTAAAGGAGCCACCCGCAGGGCCAGCTCAGCCCTGGGGGGGTACCCACAGAATC
ATGAGGGACAGTGGGCTGTTTGGACAGTACCTCCTCACACCAGCCCGAGAGTCACTGTTCCTCATCAATGGGAGACAAAA
CACGCTGCGGTGTGAGGTGTCAGGTATAAAGGGGGGGACCACAGTGGTGTGGGTGGGTGAGGTATGAAGGGCCCAGAGCA
GAGCCCTGGGCCAAGGAACACCCCCTAGTCCTGACACTGCAGCCTCAAGCAGGTACGCTGTACATTTTTACAGACAAAAG
CAAAAACCTGTACTCGCTTTGTGGTTCAACACTGGTCTCCTTGCAAGTTTCCTAGTATAAGGTATGCGCTGCTACCAAGA
TTGGGGTTTTTTCGTTAGGAAGTATGATTTATGCCTTGAGCTACGATGAGAACATATGCTGCTGTGTAAAGGGATCATTT
CTGTGCCAAGCTGCACACCGAGTGACCTGGGGACATCATGGAACCAAGGGATCCTGCTCTCCAAGCAGACACCTCTGTCA
GTTGCCTTCACATAGTCATTGTCCCTTACTGCCAGACCCAGCCAGACTTTGCCCTGACGGAGTGGCCCGGAAGCAGAGGC
CGACCAGGAGCAGGGGCCTCCCTCCCGAACTGAAAGCCCATCCGTCCTCGCGTGGGACCGCATCTTCTCCCTCGCAGCTG
CTTCTTGCTTTTCTTTCCATTTGACTTGCTGTAAGCCTGAGGGAGAGCCAACAAGACTTACTGCATCTTGGGGGATGGGG
AAATCACTCACTTTATTTTGGAAATTTTTGATTAAAAAAAAATTTTATAATCTCAAATGCTAGTAAGCAGAAAGATGCTC
TCCGAGGTCCAACTATATCCTTCCCTGCCTTAGGCCGAGTCTCGGGGGTGGTCACAACCCCACATCCCACAGCCAGAAAG
AACAATGGTCATCTGAGAATACTGGCCCTGTCGACTATTGCCACCCTGCTTCTCCAAGAGCAGACCAGGCCACCTCATCC
GTAAGGACTCGGTTCTGTGTTGGGACCCCAAAAAACCAGAACAAGTTCTGTGTGCCTCCTTTCAGCACAGAAGGGAGACA
TCTCATTAGTCAGGTCTGGTACCCCAGATTCAGGGCAGACTGGGCTTGCCTGGCAAGGTATGGGTGGCCTCCAGGCTCAA
TGCAGAAACCCCAAGGACACGAGTGGGGCCAGGTGAGTTCCTGAAGCTATACCTTTTCAAAACAGATTTTGTTTTCCTAC
CTGTGGCCCATCCACTCCTCTCTGGTACCCCATCCCCGCATCAGCACTGCAGAGAGAACACATTTCGGCGAGGGTTTTCT
TACCCACATTCCCCAATCAATACACACACACTGCAGAACCCAGAACAGAAGGCCACAGGCTGGCACTACTGCATTCTCCT
TATGTGTCTCAGGCTGTGGTGACTCTCACATGGGCATCGAAGAAGTACAACCCACATAGCCCTCTGGAGACCGCCTAGAT
CAGAGACTCAGCAAAAACAGGCTCGCCTTCCCTCTCCCACATATGAGTGGAACTTACATGTGTCCTGGTTTGAATGATCA
TTTTGCAAGCCACACGGGTTGGGAGAGGTGGTCTCACCACAGACGTCTTTGCTAATTTGGCCACCTTCACCTACTGACAT
GACCAGGATTTTCCTTTGCCATTAAGGAATGAACTCTTTCAAGGAGAGGAAACCCTAGACTCTGTGTCACTCTCAACACA
CACAGCTCCTTTCACTCCTGCCTGACTGCCAAGCCACCTGCATCCCCCGCCCCAGATCTCATGAGATCAATCACTTGTAT
GTCTCACGCAACTTGGTCCACCAAACGCCTGTCCCCTGTAACTCCTAGGGGTGCGCCTAGACAGGTACGTCTGTTTTTTA
TTTTAAAAGATATGCTATGTAGATATAAGTTGAGGAAGCTCACCTCAAAAGCCTAGAATGCAGTTTCACAGTAGCTGGGA
TGCATGGATGACCCATCTCACCCCTTTTTTTTTCCTGCCTCAATATCTTGATATGTTATGTTTACTCCCAATCTCCCATT
TTTACCACTAAAATTCTCCAACTTTCATAAACTTTTTTTTGGAAAAATTTCCATTGTATCAGCCCCTGACAGAAAAAGGA
TCTCTGAGCCTAAAGGAGGAAAAGTCCCACCAACTACCAGACCAGAACACGAGCCCCTCTGGGCAGCAGGATTCCTAAGT
CAAAGACCAGTTTGACCCAAACTGGCCTTTTAAAATAATCAGGAGTGACAGAGTCAACTTCTGCAGCACCTGCTTCTCCC
CCACTGTCCCTTCCATCTTGGAATGTGTCTAAAAAAGCATAGCTGCCCTTTGCTGTCCTCAGAGTGCATTTCCTGGAGAC
GGCAGGCTTAGGTCTCACTGACAGCATGCCAGACACAACTGAATCGAAGCAGGCCTGAAGCCTAGGTCAGGGTTTCAGGA
GTCCAGCCCCAGGAGGCAAAGTCACCAATGCAGGGAGGTAAATGCCTTTTGGCAGGAAAACCAATAGAGTTGGTTGGGTG
GGGAGTCAGGGGTGGGAGGAGAAGGAGGAAGAGGAGGAAGGCCAGACTGGCCTGCCCTTTCTCCCATACTTCACCCCAGC
AGAGGTTCATGGGACACAGTTGGAAAGCCACTGGGAGGAAATGCCTCACTACAGGGGGGCCTCCTGTAGCAAGCCCAGCC
GGTAATCCTCCTAATGAACCCACAAGGTCAATTCACAACTGATATCTTAGCTATTAAAGAAGTACTGACTTTACCAAAAG
AATCATCAAGAAAGCTATTTATATAAACCCCCTCAGTCATTTTGAAATAAAATTAATTTTAC

The predicted amino acid sequence of FCTR2 protein corresponding to the foregoing nucleotide sequence is reported in Table 2B. FCTR2 was searched against other databases using SignalPep and PSort search protocols. The protein is most likely located in the mitochondrial matrix space (certainty=0.4718) and seems to have no N-terminal signal sequence. The predicted molecular weight is 90346.9 Daltons.

Table 2B. FCTR2 Protein Sequence (SEQ ID NO:4).

```
MQCDVGDGRLFRLSLKRALSSCPDLFGLSSRNELLASCGKKFCSRGSRCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCK
LHRAACLLGKRITVIHSKDCFLKGDTCTMAGYARLKNVLLALQTRLQPLQEGDSRQDPASQKRLLVESLFRDLDADGNGHLSSSEL
AQHVLKKQDLDEDLLGCSPGDLLRFDDYNSDSSLTLREFYMAFQVVQLSLAPEDRVSVTTVTVGLSTVLTCAVHGDLRPPIIWKRN
GLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPR
ITWLKNGVDVSTQMSKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVDEDISSLFIEDSARKTLANILWREEGLSVGNMFYVF
SDDGIIVIHPVDCEIQRHLKPTEKIFMSYEEICPQREKNATQPCQWVSAVNVRNRYIYVAQPALSRVLVVDIQAQKVLQSIGVDPL
PAKLSYDKSHDQVWVLSWGDVHKSRPSLQVITEASTGQSQHLIRTPFAGVDDFFIPPTNLIINHIRFGFIFNKSDPAVHKVDLETM
MPLKTIGLHHHGCVPQAMAHTHLGGYFFIQCRQDSPASAARQLLVDSVTDSVLGPNGDVTGTPHTSPDGRFIVSAAADSPWLHVQE
ITVRGEIQTLYDLQINSGISDLAFQRSFTESNQYNIYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWGGTHRIMRDSGLF
GQYLLTPARESLFLINGRQNTLRCEVSGIKGGTTVVWVGEV
```

In a BLASTN search it was also found that nucleotides 784-5502 of FCTR2 nucleic acid had 4672 of 4719 bases (99%) identical to *Homo sapiens* mRNA for KIAA1061 protein, partial cds (GenBank Acc:AB028984) (Table 2C).

Table 2C. BLASTN of FCTR2 against *Homo sapiens* mRNA for KIAA1061 protein (SEQ ID NO:46)

```
>GI|5689458|DBJ|AB028984.1|AB028984 HOMO SAPIENS MRNA FOR KIAA1061 PROTEIN, PARTIAL
CDS
          LENGTH = 4719

 SCORE = 9075 BITS (4578), EXPECT = 0.0
 IDENTITIES = 4672/4719 (99%)
 STRAND = PLUS / PLUS

QUERY: 784  AGAATGTCCTTCTGGCACTCCAGACCCGTCTGCAGCCACTCCAAGAAGGAGACAGCAGAC 843
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1    AGAATGTCCTTCTGGCACTCCAGACCCGTCTGCAGCCACTCCAAGAAGGAGACAGCAGAC 60

QUERY: 844  AAGACCCTGCCTCCCAGAAGCGCCTCCTGGTGGAATCTCTGTTCAGGGACTTAGATGCAG 903
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 61   AAGACCCTGCCTCCCAGAAGCGCCTCCTGGTGGAATCTCTGTTCAGGGACTTAGATGCAG 120

QUERY: 904  ATGGCAATGGCCACCTCAGCAGCTCCGAACTGGCTCAGCATGTGCTGAAGAAGCAGGACC 963
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 121  ATGGCAATGGCCACCTCAGCAGCTCCGAACTGGCTCAGCATGTGCTGAAGAAGCAGGACC 180

QUERY: 964  TGGATGAAGACTTACTTGGTTGCTCACCAGGTGACCTCCTCCGATTTGACGATTACAACA 1023
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 181  TGGATGAAGACTTACTTGGTTGCTCACCAGGTGACCTCCTCCGATTTGACGATTACAACA 240

QUERY: 1024 GTGACAGCTCCCTGACCCTCCGCGAGTTCTACATGGCCTTCCAAGTGGTTCAGCTCAGCC 1083
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 241  GTGACAGCTCCCTGACCCTCCGCGAGTTCTACATGGCCTTCCAAGTGGTTCAGCTCAGCC 300

QUERY: 1084 TCGCCCCCGAGGACAGGGTCAGTGTGACCACAGTGACCGTGGGGCTGAGCACAGTGCTGA 1143
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 301  TCGCCCCCGAGGACAGGGTCAGTGTGACCACAGTGACCGTGGGGCTGAGCACAGTGCTGA 360
```

```
QUERY: 1144 CCTGCGCCGTCCATGGAGACCTGAGGCCACCAATCATCTGGAAGCGCAACGGGCTCACCC 1203
SBJCT: 361  CCTGCGCCG[redacted]TGGAGACCTGAGGCCACCAATCATCTGGAAGCG[redacted]CGGGCTCACCC 420

QUERY: 1204 TGAACTTCCTGGACTTGGAAGACATCAATGACTTTGGAGAGGATGATTCCCTGTACATCA 1263
SBJCT: 421  TGAACTTCCTGGACTTGGAAGACATCAATGACTTTGGAGAGGATGATTCCCTGTACATCA 480

QUERY: 1264 CCAAGGTGACCACCATCCACATGGGCAATTACACCTGCCATGCTTCCGGCCACGAGCAGC 1323
SBJCT: 481  CCAAGGTGACCACCATCCACATGGGCAATTACACCTGCCATGCTTCCGGCCACGAGCAGC 540

QUERY: 1324 TGTTCCAGACCCACGTCCTGCAGGTGAATGTGCCGCCAGTCATCCGTGTCTATCCAGAGA 1383
SBJCT: 541  TGTTCCAGACCCACGTCCTGCAGGTGAATGTGCCGCCAGTCATCCGTGTCTATCCAGAGA 600

QUERY: 1384 GCCAGGCACAGGAGCCTGGAGTGGCAGCCAGCCTAAGATGCCATGCTGAGGGCATTCCCA 1443
SBJCT: 601  GCCAGGCACAGGAGCCTGGAGTGGCAGCCAGCCTAAGATGCCATGCTGAGGGCATTCCCA 660

QUERY: 1444 TGCCCAGAATCACTTGGCTGAAAAACGGCGTGGATGTCTCAACTCAGATGTCCAAACAGC 1503
SBJCT: 661  TGCCCAGAATCACTTGGCTGAAAAACGGCGTGGATGTCTCAACTCAGATGTCCAAACAGC 720

QUERY: 1504 TCTCCCTTTTAGCCAATGGGAGCGAACTCCACATCAGCAGTGTTCGGTATGAAGACACAG 1563
SBJCT: 721  TCTCCCTTTTAGCCAATGGGAGCGAACTCCACATCAGCAGTGTTCGGTATGAAGACACAG 780

QUERY: 1564 GGGCATACACCTGCATTGCCAAAAATGAAGTGGGTGTGGATGAAGATATCTCCTCGCTCT 1623
SBJCT: 781  GGGCATACACCTGCATTGCCAAAAATGAAGTGGGTGTGGATGAAGATATCTCCTCGCTCT 840

QUERY: 1624 TCATTGAAGACTCAGCTAGAAAGACCCTTGCAAACATCCTGTGGCGAGAGGAAGGCCTCA 1683
SBJCT: 841  TCATTGAAGACTCAGCTAGAAAGACCCTTGCAAACATCCTGTGGCGAGAGGAAGGCCTCA 900

QUERY: 1684 GCGTGGGAAACATGTTCTATGTCTTCTCCGACGACGGTATCATCGTCATCCATCCTGTGG 1743
SBJCT: 901  GCGTGGGAAACATGTTCTATGTCTTCTCCGACGACGGTATCATCGTCATCCATCCTGTGG 960

QUERY: 1744 ACTGTGAGATCCAGAGGCACCTCAAACCCACGGAAAAGATTTTCATGAGCTATGAAGAAA 1803
SBJCT: 961  ACTGTGAGATCCAGAGGCACCTCAAACCCACGGAAAAGATTTTCATGAGCTATGAAGAAA 1020

QUERY: 1804 TCTGTCCTCAAAGAGNNNNNNNTGCAACCCAGCCCTGCCAGTGGGTATCTGCAGTCAATG 1863
SBJCT: 1021 TCTGTCCTCAAAGAGAAAAAAATGCAACCCAGCCCTGCCAGTGGGTATCTGCAGTCAATG 1080

QUERY: 1864 TCCGGAACCGGTACATCTATGTGGCCCAGCCAGCACTGAGCAGAGTCCTTGTGGTCGACA 1923
SBJCT: 1081 TCCGGAACCGGTACATCTATGTGGCCCAGCCAGCACTGAGCAGAGTCCTTGTGGTCGACA 1140

QUERY: 1924 TCCAAGCCCAGAAAGTCCTACAGTCCATAGGTGTGGACCCTCTGCCGGCTAAGCTGTCCT 1983
SBJCT: 1141 TCCAAGCCCAGAAAGTCCTACAGTCCATAGGTGTGGACCCTCTGCCGGCTAAGCTGTCCT 1200

QUERY: 1984 ATGACAAGTCACATGACCAAGTGTGGGTCCTGAGCTGGGGGGACGTGCACAAGTCCCGAC 2043
SBJCT: 1201 ATGACAAGTCACATGACCAAGTGTGGGTCCTGAGCTGGGGGGACGTGCACAAGTCCCGAC 1260

QUERY: 2044 CAAGTCTCCAGGTGATCACAGAAGCCAGCACCGGCCAGAGCCAGCACCTCATCCGCACAC 2103
SBJCT: 1261 CAAGTCTCCAGGTGATCACAGAAGCCAGCACCGGCCAGAGCCAGCACCTCATCCGCACAC 1320

QUERY: 2104 CCTTTGCAGGAGTGGATGATTTCTTCATTCCCCCAACAAACCTCATCATCAACCACATCA 2163
SBJCT: 1321 CCTTTGCAGGAGTGGATGATTTCTTCATTCCCCCAACAAACCTCATCATCAACCACATCA 1380

QUERY: 2164 GGTTTGGCTTCATCTTCAACAAGTCTGATCCTGCAGTCCACAAGGTGGACCTGGAAACAA 2223
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SBJCT: 1381 GGTTTGGCTTCATCTTCAACAAGTCTGATCCTGCAGTCCACAAGGTGGACCTGGAAACAA 1440

QUERY: 2224 TGATGCCCC GACCATCGGCCTGCACCACCATGGCTGCGTGCC GGCCATGGCAC 2283
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1441 TGATGCCCCTCAAGACCATCGGCCTGCACCACCATGGCTGCGTGCCCCAGGCCATGGCAC 1500

QUERY: 2284 ACACCCACCTGGGCGGCTACTTCTTCATCCAGTGCCGACAGGACAGCCCCGCCTCTGCTG 2343
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1501 ACACCCACCTGGGCGGCTACTTCTTCATCCAGTGCCGACAGGACAGCCCCGCCTCTGCTG 1560

QUERY: 2344 CCCGACAGCTGCTCGTTGACAGTGTCACAGACTCTGTGCTTGGCCCCAATGGTGATGTAA 2403
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1561 CCCGACAGCTGCTCGTTGACAGTGTCACAGACTCTGTGCTTGGCCCCAATGGTGATGTAA 1620

QUERY: 2404 CAGGCACCCCACACACATCCCCCGACGGGCGCTTCATAGTCAGTGCTGCAGCTGACAGCC 2463
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1621 CAGGCACCCCACACACATCCCCCGACGGGCGCTTCATAGTCAGTGCTGCAGCTGACAGCC 1680

QUERY: 2464 CCTGGCTGCACGTGCAGGAGATCACAGTGCGGGGCGAGATCCAGACCCTGTATGACCTGC 2523
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1681 CCTGGCTGCACGTGCAGGAGATCACAGTGCGGGGCGAGATCCAGACCCTGTATGACCTGC 1740

QUERY: 2524 AAATAAACTCGGGCATCTCAGACTTGGCCTTCCAGCGCTCCTTCACTGAAAGCAATCAAT 2583
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1741 AAATAAACTCGGGCATCTCAGACTTGGCCTTCCAGCGCTCCTTCACTGAAAGCAATCAAT 1800

QUERY: 2584 ACAACATCTACGCGGCTCTGCACACGGAGCCGGACCTGCTGTTCCTGGAGCTGTCCACGG 2643
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1801 ACAACATCTACGCGGCTCTGCACACGGAGCCGGACCTGCTGTTCCTGGAGCTGTCCACGG 1860

QUERY: 2644 GGAAGGTGGGCATGCTGAAGAACTTAAAGGAGCCACCCGCAGGGCCAGCTCAGCCCTNNN 2703
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1861 GGAAGGTGGGCATGCTGAAGAACTTAAAGGAGCCACCCGCAGGGCCAGCTCAGCCCTGGG 1920

QUERY: 2704 NNNNTACCCACAGAATCATGAGGGACAGTGGGCTGTTTGGACAGTACCTCCTCACACCAG 2763
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1921 GGGGTACCCACAGAATCATGAGGGACAGTGGGCTGTTTGGACAGTACCTCCTCACACCAG 1980

QUERY: 2764 CCCGAGAGTCACTGTTCCTCATCAATGGGAGACAAAACACGCTGCGGTGTGAGGTGTCAG 2823
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1981 CCCGAGAGTCACTGTTCCTCATCAATGGGAGACAAAACACGCTGCGGTGTGAGGTGTCAG 2040

QUERY: 2824 GTATAAANNNNNNNACCACAGTGGTGTGGGTGGGTGAGGTATGAAGGGCCCAGAGCAGAG 2883
           |||||||      ||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 2041 GTATAAAGGGGGGGACCACAGTGGTGTGGGTGGGTGAGGTATGAAGGGCCCAGAGCAGAG 2100

QUERY: 2884 CCCTGGGCCAAGGAACACCCCCTAGTCCTGACACTGCAGCCTCAAGCAGGTACGCTGTAC 2943
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 2101 CCCTGGGCCAAGGAACACCCCCTAGTCCTGACACTGCAGCCTCAAGCAGGTACGCTGTAC 2160

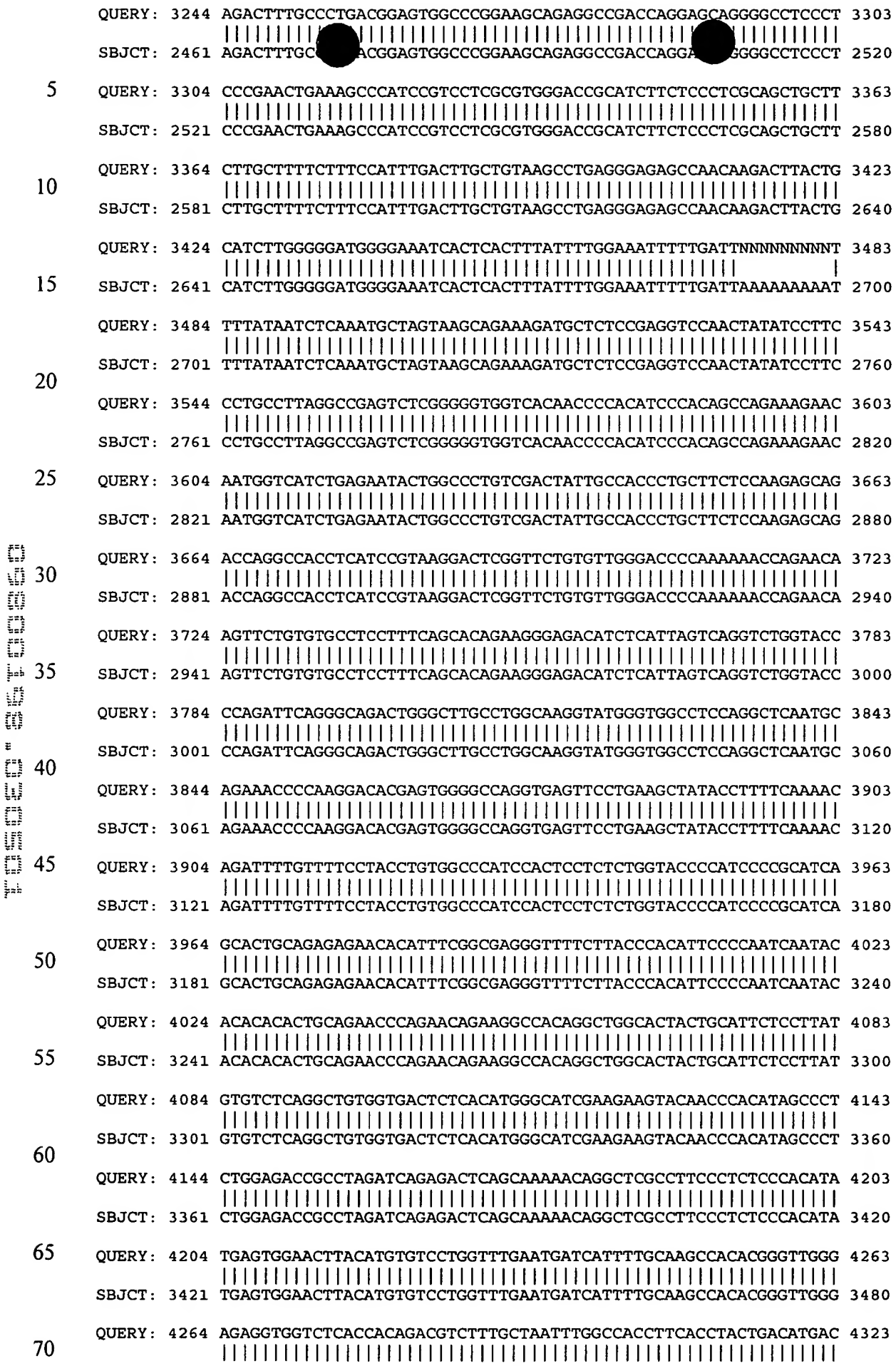
QUERY: 2944 ATTTTTACAGACAAAAGCAAAAACCTGTACTCGCTTTGTGGTTCAACACTGGTCTCCTTG 3003
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 2161 ATTTTTACAGACAAAAGCAAAAACCTGTACTCGCTTTGTGGTTCAACACTGGTCTCCTTG 2220

QUERY: 3004 CAAGTTTCCTAGTATAAGGTATGCGCTGCTACCAAGATTGGGGTTTTTTCGTTAGGAAGT 3063
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 2221 CAAGTTTCCTAGTATAAGGTATGCGCTGCTACCAAGATTGGGGTTTTTTCGTTAGGAAGT 2280

QUERY: 3064 ATGATTTATGCCTTGAGCTACGATGAGAACATATGCTGCTGTGTAAAGGGATCATTTCTG 3123
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 2281 ATGATTTATGCCTTGAGCTACGATGAGAACATATGCTGCTGTGTAAAGGGATCATTTCTG 2340

QUERY: 3124 TGCCAAGCTGCACACCGAGTGACCTGGGGACATCATGGAACCAAGGGATCCTGCTCTCCA 3183
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 2341 TGCCAAGCTGCACACCGAGTGACCTGGGGACATCATGGAACCAAGGGATCCTGCTCTCCA 2400

QUERY: 3184 AGCAGACACCTCTGTCAGTTGCCTTCACATAGTCATTGTCCCTTACTGCCAGACCCAGCC 3243
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 2401 AGCAGACACCTCTGTCAGTTGCCTTCACATAGTCATTGTCCCTTACTGCCAGACCCAGCC 2460
```


QUERY: 3244 AGACTTTGCCCTGACGGAGTGGCCCGGAAGCAGAGGCCGACCAGGAGCAGGGGCCTCCCT 3303
SBJCT: 2461 AGACTTTGC[redacted]ACGGAGTGGCCCGGAAGCAGAGGCCGACCAGGA[redacted]GGGGCCTCCCT 2520
QUERY: 3304 CCCGAACTGAAAGCCCATCCGTCCTCGCGTGGGACCGCATCTTCTCCCTCGCAGCTGCTT 3363
SBJCT: 2521 CCCGAACTGAAAGCCCATCCGTCCTCGCGTGGGACCGCATCTTCTCCCTCGCAGCTGCTT 2580
QUERY: 3364 CTTGCTTTTCTTTCCATTTGACTTGCTGTAAGCCTGAGGGAGAGCCAACAAGACTTACTG 3423
SBJCT: 2581 CTTGCTTTTCTTTCCATTTGACTTGCTGTAAGCCTGAGGGAGAGCCAACAAGACTTACTG 2640
QUERY: 3424 CATCTTGGGGGATGGGGAAATCACTCACTTTATTTTGGAAATTTTTGATTNNNNNNNNNT 3483
SBJCT: 2641 CATCTTGGGGGATGGGGAAATCACTCACTTTATTTTGGAAATTTTTGATTAAAAAAAAAT 2700
QUERY: 3484 TTTATAATCTCAAATGCTAGTAAGCAGAAAGATGCTCTCCGAGGTCCAACTATATCCTTC 3543
SBJCT: 2701 TTTATAATCTCAAATGCTAGTAAGCAGAAAGATGCTCTCCGAGGTCCAACTATATCCTTC 2760
QUERY: 3544 CCTGCCTTAGGCCGAGTCTCGGGGGTGGTCACAACCCCACATCCCACAGCCAGAAAGAAC 3603
SBJCT: 2761 CCTGCCTTAGGCCGAGTCTCGGGGGTGGTCACAACCCCACATCCCACAGCCAGAAAGAAC 2820
QUERY: 3604 AATGGTCATCTGAGAATACTGGCCCTGTCGACTATTGCCACCCTGCTTCTCCAAGAGCAG 3663
SBJCT: 2821 AATGGTCATCTGAGAATACTGGCCCTGTCGACTATTGCCACCCTGCTTCTCCAAGAGCAG 2880
QUERY: 3664 ACCAGGCCACCTCATCCGTAAGGACTCGGTTCTGTGTTGGGACCCCAAAAAACCAGAACA 3723
SBJCT: 2881 ACCAGGCCACCTCATCCGTAAGGACTCGGTTCTGTGTTGGGACCCCAAAAAACCAGAACA 2940
QUERY: 3724 AGTTCTGTGTGCCTCCTTTCAGCACAGAAGGGAGACATCTCATTAGTCAGGTCTGGTACC 3783
SBJCT: 2941 AGTTCTGTGTGCCTCCTTTCAGCACAGAAGGGAGACATCTCATTAGTCAGGTCTGGTACC 3000
QUERY: 3784 CCAGATTCAGGGCAGACTGGGCTTGCCTGGCAAGGTATGGGTGGCCTCCAGGCTCAATGC 3843
SBJCT: 3001 CCAGATTCAGGGCAGACTGGGCTTGCCTGGCAAGGTATGGGTGGCCTCCAGGCTCAATGC 3060
QUERY: 3844 AGAAACCCCAAGGACACGAGTGGGGCCAGGTGAGTTCCTGAAGCTATACCTTTTCAAAAC 3903
SBJCT: 3061 AGAAACCCCAAGGACACGAGTGGGGCCAGGTGAGTTCCTGAAGCTATACCTTTTCAAAAC 3120
QUERY: 3904 AGATTTTGTTTTCCTACCTGTGGCCCATCCACTCCTCTCTGGTACCCCATCCCCGCATCA 3963
SBJCT: 3121 AGATTTTGTTTTCCTACCTGTGGCCCATCCACTCCTCTCTGGTACCCCATCCCCGCATCA 3180
QUERY: 3964 GCACTGCAGAGAGAACACATTTCGGCGAGGGTTTTCTTACCCACATTCCCCAATCAATAC 4023
SBJCT: 3181 GCACTGCAGAGAGAACACATTTCGGCGAGGGTTTTCTTACCCACATTCCCCAATCAATAC 3240
QUERY: 4024 ACACACACTGCAGAACCCAGAACAGAAGGCCACAGGCTGGCACTACTGCATTCTCCTTAT 4083
SBJCT: 3241 ACACACACTGCAGAACCCAGAACAGAAGGCCACAGGCTGGCACTACTGCATTCTCCTTAT 3300
QUERY: 4084 GTGTCTCAGGCTGTGGTGACTCTCACATGGGCATCGAAGAAGTACAACCCACATAGCCCT 4143
SBJCT: 3301 GTGTCTCAGGCTGTGGTGACTCTCACATGGGCATCGAAGAAGTACAACCCACATAGCCCT 3360
QUERY: 4144 CTGGAGACCGCCTAGATCAGAGACTCAGCAAAAACAGGCTCGCCTTCCCTCTCCCACATA 4203
SBJCT: 3361 CTGGAGACCGCCTAGATCAGAGACTCAGCAAAAACAGGCTCGCCTTCCCTCTCCCACATA 3420
QUERY: 4204 TGAGTGGAACTTACATGTGTCCTGGTTTGAATGATCATTTTGCAAGCCACACGGGTTGGG 4263
SBJCT: 3421 TGAGTGGAACTTACATGTGTCCTGGTTTGAATGATCATTTTGCAAGCCACACGGGTTGGG 3480
QUERY: 4264 AGAGGTGGTCTCACCACAGACGTCTTTGCTAATTTGGCCACCTTCACCTACTGACATGAC 4323

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SBJCT: 3481 AGAGGTGGTCTCACCACAGACGTCTTTGCTAATTTGGCCACCTTCACCTACTGACATGAC 3540

QUERY: 4324 CAGGATTTT[redacted]TGCCATTAAGGAATGAACTCTTTCAAGGAGAGG[redacted]CCTAGACTCT 4383
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 3541 CAGGATTTTCCTTTGCCATTAAGGAATGAACTCTTTCAAGGAGAGGAAACCCTAGACTCT 3600

QUERY: 4384 GTGTCACTCTCAACACACACAGCTCCTTTCACTCCTGCCTGACTGCCAAGCCACCTGCAT 4443
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 3601 GTGTCACTCTCAACACACACAGCTCCTTTCACTCCTGCCTGACTGCCAAGCCACCTGCAT 3660

QUERY: 4444 CCCCCGCCCCAGATCTCATGAGATCAATCACTTGTATGTCTCACGCAACTTGGTCCACCA 4503
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 3661 CCCCCGCCCCAGATCTCATGAGATCAATCACTTGTATGTCTCACGCAACTTGGTCCACCA 3720

QUERY: 4504 AACGCCTGTCCCCTGTAACTCCTAGGGGTGCGCCTAGACAGGTACGTCTGTTTTTTATTT 4563
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 3721 AACGCCTGTCCCCTGTAACTCCTAGGGGTGCGCCTAGACAGGTACGTCTGTTTTTTATTT 3780

QUERY: 4564 TAAAAGATATGCTATGTAGATATAAGTTGAGGAAGCTCACCTCAAAAGCCTAGAATGCAG 4623
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 3781 TAAAAGATATGCTATGTAGATATAAGTTGAGGAAGCTCACCTCAAAAGCCTAGAATGCAG 3840

QUERY: 4624 TTTCACAGTAGCTGGGATGCATGGATGACCCATCTCACCCCNNNNNNNNNCCTGCCTCAA 4683
           ||||||||||||||||||||||||||||||||||||||||||          ||||||||||
SBJCT: 3841 TTTCACAGTAGCTGGGATGCATGGATGACCCATCTCACCCCTTTTTTTTTCCTGCCTCAA 3900

QUERY: 4684 TATCTTGATATGTTATGTTTACTCCCAATCTCCCATTTTTACCACTAAAATTCTCCAACT 4743
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 3901 TATCTTGATATGTTATGTTTACTCCCAATCTCCCATTTTTACCACTAAAATTCTCCAACT 3960

QUERY: 4744 TTCATAAACNNNNNNNNGGAAAAATTTCCATTGTATCAGCCCCTGACAGAAAAAGGATCT 4803
           |||||||||         ||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 3961 TTCATAAACTTTTTTTTGGAAAAATTTCCATTGTATCAGCCCCTGACAGAAAAAGGATCT 4020

QUERY: 4804 CTGAGCCTAAAGGAGGAAAAGTCCCACCAACTACCAGACCAGAACACGAGCCCCTCTGGG 4863
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 4021 CTGAGCCTAAAGGAGGAAAAGTCCCACCAACTACCAGACCAGAACACGAGCCCCTCTGGG 4080

QUERY: 4864 CAGCAGGATTCCTAAGTCAAAGACCAGTTTGACCCAAACTGGCCTTTTAAAATAATCAGG 4923
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 4081 CAGCAGGATTCCTAAGTCAAAGACCAGTTTGACCCAAACTGGCCTTTTAAAATAATCAGG 4140

QUERY: 4924 AGTGACAGAGTCAACTTCTGCAGCACCTGCTTCTCCCCCACTGTCCCTTCCATCTTGGAA 4983
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 4141 AGTGACAGAGTCAACTTCTGCAGCACCTGCTTCTCCCCCACTGTCCCTTCCATCTTGGAA 4200

QUERY: 4984 TGTGTCTAAAAAAGCATAGCTGCCCTTTGCTGTCCTCAGAGTGCATTTCCTGGAGACGGC 5043
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 4201 TGTGTCTAAAAAAGCATAGCTGCCCTTTGCTGTCCTCAGAGTGCATTTCCTGGAGACGGC 4260

QUERY: 5044 AGGCTTAGGTCTCACTGACAGCATGCCAGACACAACTGAATCGAAGCAGGCCTGAAGCCT 5103
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 4261 AGGCTTAGGTCTCACTGACAGCATGCCAGACACAACTGAATCGAAGCAGGCCTGAAGCCT 4320

QUERY: 5104 AGGTCAGGGTTTCAGGAGTCCAGCCCCAGGAGGCAAAGTCACCAATGCAGGGAGGTAAAT 5163
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 4321 AGGTCAGGGTTTCAGGAGTCCAGCCCCAGGAGGCAAAGTCACCAATGCAGGGAGGTAAAT 4380

QUERY: 5164 GCCTTTTGGCAGGAAAACCAATAGAGTTGGTTGGGTGGGGAGTCAGGGGTGGGAGGAGAA 5223
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 4381 GCCTTTTGGCAGGAAAACCAATAGAGTTGGTTGGGTGGGGAGTCAGGGGTGGGAGGAGAA 4440

QUERY: 5224 GGAGGAAGAGGAGGAAGGCCAGACTGGCCTGCCCTTTCTCCCATACTTCACCCCAGCAGA 5283
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 4441 GGAGGAAGAGGAGGAAGGCCAGACTGGCCTGCCCTTTCTCCCATACTTCACCCCAGCAGA 4500

QUERY: 5284 GGTTCATGGGACACAGTTGGAAAGCCACTGGGAGGAAATGCCTCACTACAGGGGGGCCTC 5343
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 4501 GGTTCATGGGACACAGTTGGAAAGCCACTGGGAGGAAATGCCTCACTACAGGGGGGCCTC 4560
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QUERY: 5344 CTGTAGCAAGCCCAGCCGGTAATCCTCCTAATGAACCCACAAGGTCAATTCACAACTGAT 5403
           ||||||||||[ ]||||||||||||||||||||||||||||||||||[ ]||||||||||
SBJCT: 4561 CTGTAGCAA[ ]AGCCGGTAATCCTCCTAATGAACCCACAAGGTC[ ]TCACAACTGAT 4620

QUERY: 5404 ATCTTAGCTATTAAAGAAGTACTGACTTTACCAAAAGAATCATCAAGAAAGCTATTTATA 5463
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 4621 ATCTTAGCTATTAAAGAAGTACTGACTTTACCAAAAGAATCATCAAGAAAGCTATTTATA 4680

QUERY: 5464 TAAACCCCCTCAGTCATTTTGAAATAAAATTAATTTTAC 5502
           |||||||||||||||||||||||||||||||||||||
SBJCT: 4681 TAAACCCCCTCAGTCATTTTGAAATAAAATTAATTTTAC 4719
```

The FCTR2 amino acid sequence has 473 of 810 amino acid residues (58%) identical to, and 616 of 810 residues (76%) positive with, the 850 amino acid residue proteins from *Homo sapiens* KIAA1263 Protein fragment (ptnr: TREMBLNEW-ACC:BAA86577) (SEQ ID NO:47) (Table 2D).

Table 2D. BLASTP of FCTR2 against *Homo sapiens* KIAA1263 Protein fragment (SEQ ID NO:47)

```
ptnr:TREMBLNEW-ACC:BAA86577 KIAA1263 PROTEIN - Homo sapiens (Human), 850 aa
(fragment)
   Length = 850

 Score = 2573 (905.7 bits), Expect = 2.0e-267, P = 2.0e-267
 Identities = 473/810 (58%), Positives = 616/810 (76%)

QUERY: 10  LFRLSLKRALSSCPDLFGLSSRNELLASCGKKFCSRGSRCVLSRKTGEPECQCLEACRPS 69
           | ||  |         + |   ++    ||  |+|  |  || ||+||+ || |++ |+
SBJCT: 40  LMRLRHKEKNQESSRVKGFMIQDGPFGSCENKYCGLGRHCVTSRETGQAECACMDLCKRH 99

QUERY: 70  YVPVCGSDGRFYENHCKLHRAACLLGKRITVIHSKDCFLKGDTCTMAGYARLKNVLLALQ 129
           | ||||||| ||||||++||||||  ++||++|++||| ||| |    |+++||+|| ||
SBJCT: 100 YKPVCGSDGEFYENHCEVHRAACLKKQKITIVHNEDCFFKGDKCKTTEYSKMKNMLLDLQ 159

QUERY: 130 TRLQPLQEGDSRQ-DPASQKRLLVESLFRDLDADGNGHLSSSELAQHVLKKQDLDEDLLG 188
            +   +|| ++    |  |+|+|||+ +|+  ||| || +  +|| | |+|+++| +||
SBJCT: 160 NQKYIMQENENPNGDDISRKKLLVDQMFKYFDADSNGLVDINELTQ-VIKQEELGKDLFD 218

QUERY: 189 CSPGDLLRFDDYNSDSSLTLREFYMAFQVVQLSLAPEDRVSVTTVTVGLSTVLTCAVHGD 248
           |+   ||++||+|+|   | | ||| ||||+|||| + + | |  ||| | || ||+ |
SBJCT: 219 CTLYVLLKYDDFNADKHLALEEFYRAFQVIQLSLPEDQKLSITAATVGQSAVLSCAIQGT 278

QUERY: 249 LRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQLFQTHVL 308
           |||||||||| + || ||||||||||+| ||||||||| |+|||||+| |+||++|||+
SBJCT: 279 LRPPIIWKRNNIILNNLDLEDINDFGDDGSLYITKVTTTHVGNYTCYADGYEQVYQTHIF 338

QUERY: 309 QVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQLSLLANG 368
           |||||||||||||||+|||| |||||||||| |++ |||||+|++ ++||||+| |||
SBJCT: 339 QVNVPPVIRVYPESQAREPGVTASLRCHAEGIPKPQLGWLKNGIDITPKLSKQLTLQANG 398

QUERY: 369 SELHISSVRYEDTGAYTCIAKNEVGVDEDISSLFIEDSARKTLANILWREEGLSVGNMFY 428
           ||+|||+|||||||||||||||| |||||||||+|||||||||||||||||| +|||||
SBJCT: 399 SEVHISNVRYEDTGAYTCIAKNEAGVDEDISSLFVEDSARKTLANILWREEGLGIGNMFY 458

QUERY: 429 VFSDDGIIVIHPVDCEIQRHLKPTEKIFMSYEEICPQREKNATQPCQWVSAVNVRNRYIY 488
           || +||| || |++|| |||+||+||+    +|+||+ | +  | | | |||||++++||
SBJCT: 459 VFYEDGIKVIQPIECEFQRHIKPSEKLLGFQDEVCPKAEGDEVQRCVWASAVNVKDKFIY 518

QUERY: 489 VAQPALSRVLVVDIQAQKVLQSIGVDPLPAKLSYDKSHDQVWVLSWGDVHKSRPSLQVIT 548
           |||| | |||+||+|+|||+|++  ||+| || ||||||||||||| + |+ |+|||||
SBJCT: 519 VAQPTLDRVLIVDVQSQKVVQAVSTDPVPVKLHYDKSHDQVWVLSWGTLEKTSPTLQVIT 578

QUERY: 549 EASTGQSQHLIRT-----PFAGVDDFFIPPTNLIINHIRFGFIFNKSDPAVHKVDLETMM 603
```

```
SBJCT: 579 LASGNVPHHT[redacted]PVGKQFDRVDDFFIPTTTLIITHMRFGFILHKD[redacted]QKIDLETMS 638

QUERY: 604 PLKTIGLHHHGCVPQAMAHTHLGGYFFIQCRQDSPASAARQLLVDSVTDSVLGPNGDVTG 663

SBJCT: 639 YIKTINLKDYKCVPQSLAYTHLGGYYFIGCKPDSTGAVSPQVMVDGVTDSVIGFNSDVTG 698

QUERY: 664 TPHTSPDGRFIVSAAADSPWLHVQEITVRGEIQTLYDLQINSGISDLAFQRSFTESNQYN 723

SBJCT: 699 TPYVSPDGHYLVSINDVKGLVRVQYITIRGEIQEAFDIYTNLHISDLAFQPSFTEAHQYN 758

QUERY: 724 IYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWGGTHRIMRDSGLFGQYLLTPAR 783

SBJCT: 759 IYGSSSTQTDVLFVELSSGKVKMIKSLKEPLKAEEWPWNRKNRQIQDSGLFGQYLMTPSK 818

QUERY: 784 ESLFLINGRQNTLRCEVSGIKGGTTVVWVGE 814

SBJCT: 819 DSLFILDGRLNKLNCEITEVEKGNTVIWVGD 849
```

Amino acids 123-815 of FCTR2 also have 693 of 693 amino acid residues (100%) identical to,the 693 amino acid residue protein fragment of KIAA1061 Protein from *Homo sapiens* (ptnr: TREMBLNEW-ACC: BAA83013) (SEQ ID NO:48) (Table 2E).

Table 2E. BLASTP of FCTR2 against KIAA1061 Protein [Fragment] (SEQ ID NO:48)

ptnr:TREMBLNEW-ACC:BAA83013 KIAA1061 PROTEIN - Homo sapiens (Human), 693 aa (fragment).

```
           Length = 693

 Score = 3623 (1275.4 bits), Expect = 0.0, P = 0.0
 Identities = 693/693 (100%), Positives = 693/693 (100%)

QUERY: 123 NVLLALQTRLQPLQEGDSRQDPASQKRLLVESLFRDLDADGNGHLSSSELAQHVLKKQDL 182

SBJCT: 1   NVLLALQTRLQPLQEGDSRQDPASQKRLLVESLFRDLDADGNGHLSSSELAQHVLKKQDL 60

QUERY: 183 DEDLLGCSPGDLLRFDDYNSDSSLTLREFYMAFQVVQLSLAPEDRVSVTTVTVGLSTVLT 242

SBJCT: 61  DEDLLGCSPGDLLRFDDYNSDSSLTLREFYMAFQVVQLSLAPEDRVSVTTVTVGLSTVLT 120

QUERY: 243 CAVHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQL 302

SBJCT: 121 CAVHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQL 180

QUERY: 303 FQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQL 362

SBJCT: 181 FQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQL 240

QUERY: 363 SLLANGSELHISSVRYEDTGAYTCIAKNEVGVDEDISSLFIEDSARKTLANILWREEGLS 422

SBJCT: 241 SLLANGSELHISSVRYEDTGAYTCIAKNEVGVDEDISSLFIEDSARKTLANILWREEGLS 300

QUERY: 423 VGNMFYVFSDDGIIVIHPVDCEIQRHLKPTEKIFMSYEEICPQREKNATQPCQWVSAVNV 482

SBJCT: 301 VGNMFYVFSDDGIIVIHPVDCEIQRHLKPTEKIFMSYEEICPQREKNATQPCQWVSAVNV 360

QUERY: 483 RNRYIYVAQPALSRVLVVDIQAQKVLQSIGVDPLPAKLSYDKSHDQVWVLSWGDVHKSRP 542

SBJCT: 361 RNRYIYVAQPALSRVLVVDIQAQKVLQSIGVDPLPAKLSYDKSHDQVWVLSWGDVHKSRP 420

QUERY: 543 SLQVITEASTGQSQHLIRTPFAGVDDFFIPPTNLIINHIRFGFIFNKSDPAVHKVDLETM 602

SBJCT: 421 SLQVITEASTGQSQHLIRTPFAGVDDFFIPPTNLIINHIRFGFIFNKSDPAVHKVDLETM 480
```

```
QUERY: 603 MPLKTIGLHH[redacted]PQAMAHTHLGGYFFIQCRQDSPASAARQLLVDS[redacted]SVLGPNGDVT 662
           ||||||||||[redacted]||||||||||||||||||||||||||||||||||||[redacted]||||||||||
SBJCT: 481 MPLKTIGLHHHGCVPQAMAHTHLGGYFFIQCRQDSPASAARQLLVDSVTDSVLGPNGDVT 540

QUERY: 663 GTPHTSPDGRFIVSAAADSPWLHVQEITVRGEIQTLYDLQINSGISDLAFQRSFTESNQY 722
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 541 GTPHTSPDGRFIVSAAADSPWLHVQEITVRGEIQTLYDLQINSGISDLAFQRSFTESNQY 600

QUERY: 723 NIYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWGGTHRIMRDSGLFGQYLLTPA 782
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 601 NIYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWGGTHRIMRDSGLFGQYLLTPA 660

QUERY: 783 RESLFLINGRQNTLRCEVSGIKGGTTVVWVGEV 815
           |||||||||||||||||||||||||||||||||
SBJCT: 661 RESLFLINGRQNTLRCEVSGIKGGTTVVWVGEV 693
```

The amino acid sequence of the FCTR2 protein has 451 of 772 amino acid residues (58%) identical to, and 586 of 772 residues (75%) positive with, the 773 amino acid residue proteins hypothetical protein DKFZp566D234.1 from *Homo sapiens* (fragments) (ptnr: SPTREMBL-ACC: CAB70877.1) (SEQ ID NO:49) (Table 2F).

Table 2F. BLASTP of FCTR2 against hypothetical protein DKFZp566D234.1 (SEQ ID NO:49)

```
>GI|11360192|PIR||T46283 HYPOTHETICAL PROTEIN DKFZP566D234.1 - HUMAN (FRAGMENTS)
 GI|6808053|EMB|CAB70877.1| (AL137695) HYPOTHETICAL PROTEIN [HOMO SAPIENS]
          LENGTH = 773

 SCORE =  911 BITS (2354), EXPECT = 0.0
 IDENTITIES = 451/772 (58%), POSITIVES = 586/772 (75%), GAPS = 7/772 (0%)

QUERY: 49  CVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKRITVIHSKDCFL 108
           || ||+||+ || |++ |+  | ||||||| ||||||++|||||| ++||++|++|||
SBJCT: 2   CVTSRETGQAECACMDLCKRHYKPVCGSDGEFYENHCEVHRAACLKKQKITIVHNEDCFF 61

QUERY: 109 KGDTCTMAGYARLKNVLLALQTRLQPLQEGDSRQ-DPASQKRLLVESLFRDLDADGNGHL 167
           ||| |     +++||+|| || +   +|| ++    |  |+|+|||+ +|+  ||| |  +
SBJCT: 62  KGDKCKTTECSKMKNMLLDLQNQRYIMQENENPNGDDISRKKLLVDQMFKYFDADSNDLV 121

QUERY: 168 SSSELAQHVLKKQDLDEDLLGCSPGDLLRFDDYNSDSSLTLREFYMAFQVVQLSLAPEDR 227
             +|| | |+|+++| +||  |+   ||++||+|+|  | | ||| ||||+|||| + +
SBJCT: 122 DINELTQ-VIKQEELGKDLFDCTLYVLLKYDDFNADKHLALEEFYRAFQVIQLSLPEDQK 180

QUERY: 228 XXXXXXXXXXXXXXXCAVHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTI 287
                        ||+ | |||||||||| + || | ||||||||+| |||||||||
SBJCT: 181 LSITAATVGQSAVLSCAIQGTLRPPIIWKRNNIILNNLGLEDINDFGDDGSLYITKVTTT 240

QUERY: 288 HMGNYTCHASGHEQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITW 347
           |+|||||+| |+||++|||+ |||||||||||||||+|||| |||||||||| |++ |
SBJCT: 241 HVGNYTCYADGYEQVYQTHIFQVNVPPVIRVYPESQAREPGVTASLRCHAEGIPKPQLGW 300

QUERY: 348 LKNGVDVSTQMSKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVDEDISSLFIEDSA 407
           ||||+|++ ++||||+| |||||+|||+|||||||||||||| ||||||||||+||||
SBJCT: 301 LKNGIDITPKLSKQLTLQANGSEVHISNVRYEDTGAYTCIAKNEAGVDEDISSLFVEDSA 360

QUERY: 408 RKTLANILWREEGLSVGNMFYVFSDDGIIVIHPVDCEIQRHLKPTEKIFMSYEEICPQRE 467
           |||||||||||||| +|||||| +||| || |++|| |||+||+||+    +|+||  |
SBJCT: 361 RKTLANILWREEGLGIGNMFYVFYEDGIKVIQPIECEFQRHIKPSEKLLGFQDEVCPIAE 420

QUERY: 468 KNATQPCQWVSAVNVRNRYIYVAQPALSRVLVVDIQAQKVLQSIGVDPLPAKLSYDKSHD 527
            +  | | | |||||++++|||||| | |||+||+|+|||+|++  ||+| || ||||||
SBJCT: 421 GDEVQRCVWASAVNVKDKFIYVAQPTLDRVLIVDVQSQKVVQAVSTDPVPVKLHYDKSHD 480
```

```
QUERY: 528 QVWVLSWGDVHKSRPSLQVITEASTGQSQHLIRT-----PFAGVDDFFIPPTNLIINHIR 582
SBJCT: 481 QVWVLSWGTL[redacted]PTLQVITLASGNVPHHTIHTQPVGKQFDRVDD[redacted]TTLIITHMR 540

QUERY: 583 FGFIFNKSDPAVHKVDLETMMPLKTIGLHHHGCVPQAMAHTHLGGYFFIQCRQDSPASAA 642
SBJCT: 541 FGFILHKDEAALQKIDLETMSYIKTINLKDYKCVPQSLAYTHLGGYYFIGCKPDSTGAVS 600

QUERY: 643 RQLLVDSVTDSVLGPNGDVTGTPHTSPDGRFIVSAAADSPWLHVQEITVRGEIQTLYDLQ 702
SBJCT: 601 PQVMVDGVTDSVIGFNSDVTGTPYVSPDGHYLVSINDVKGLVRVQYITIRGEIQEAFDIY 660

QUERY: 703 INSGISDLAFQRSFTESNQYNIYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWG 762
SBJCT: 661 TNLHISDLAFQPSFTEAHQYNIYGSSSTQTDVLFVELSSGKVKMIKSLKEPLKAEEWPWN 720

QUERY: 763 GTHRIMRDSGLFGQYLLTPARESLFLINGRQNTLRCEVSGIKGGTTVVWVGE 814
SBJCT: 721 RKNRQIQDSGLFGQYLMTPSKDSLFILDGRLNKLNCEITEVEKGNTVIWVGD 772
```

The amino acid sequence of the FCTR2 protein has 61 of 194 amino acid residues (31%) identical to, and 90 of 194 residues (45%) positive with, the 306 amino acid residue protein Follastin-Related Protein 1 Precursor from *Rattus Norvegicus* (ptnr: GenBank Acc:Q62632) (SEQ ID NO:50) (Table 2G).

Table 2G. BLASTP of FCTR2 against Follastatin-Related Protein 1 Precursor from *Rattus Norvegicus* (SEQ ID NO:50)

```
>GI|2498392|SP|Q62632|FRP_RAT FOLLISTATIN-RELATED PROTEIN 1 PRECURSOR
 GI|1083669|PIR||S51361 FOLLISTATIN-RELATED PROTEIN PRECURSOR - RAT
 GI|536900|GB|AAA66063.1| (U06864) FOLLISTATIN-RELATED PROTEIN PRECURSOR [RATTUS
NORVEGICUS]
          LENGTH = 306

 SCORE = 86.4 BITS (213), EXPECT = 1E-15
 IDENTITIES = 61/194 (31%), POSITIVES = 90/194 (45%), GAPS = 26/194 (13%)

QUERY: 38  CGKKFCSRGSRCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97
SBJCT: 29  CANVFCGAGRECAVTEK-GEPTCLCIEQCKPHKRPVCGSNGKTYLNHCELHRDACLTGSK 87

QUERY: 98  ITVIHSKDCFLKGD--------TCTMAGYARLKNVLLA-LQTRLQPLQEGDSRQDPASQK 148
SBJCT: 88  IQVDYDGHCKEKKSVSPSASPVVCYQANRDELRRRIIQWLEAEIIP----DGWFSKGSNY 143

QUERY: 149 RLLVESLFRDLDADGNGHLSSSELAQHVLK-----------KQDLDEDLLGCSPGDLLRF 197
SBJCT: 144 SEILDKYFKSFD-NGDSHLDSSEFLKFVEQNETAVNITAYPNQENNKLLRGLCVDALIEL 202

QUERY: 198 DDYNSDSSLTLREF 211
SBJCT: 203 SDENADWKLSFQEF 216
```

The amino acid sequence of the FCTR2 protein has 61 of 194 amino acid residues (31%) identical to, and 89 of 194 residues (45%) positive with, the 306 amino acid residue protein Follastin-Related Protein 1 Precursor from *Mus musculus* (GenBank Acc:Q62356) (SEQ ID NO:51) (Table 2H).

Table 2H. BLASTP of FCTR2 against Follastatin-Related Protein 1 Precursor from *Mus musculus* (SEQ ID NO:51)

```
>GI|6679871|REF|NP_032073.1| FOLLISTATIN-LIKE [MUS MUSCULUS]
 GI|2498391|SP|Q62356|FRP_MOUSE FOLLISTATIN-RELATED PROTEIN 1 PRECURSOR (TGF-BETA-
INDUCIBLE PROTEIN
           TSC-36)
 GI|481186|PIR||S38251 FOLLISTATIN-RELATED PROTEIN - MOUSE
 GI|349006|GB|AAC37633.1| (M91380) TGF-BETA-INDUCIBLE PROTEIN [MUS MUSCULUS]
          LENGTH = 306

 SCORE = 85.2 BITS (210), EXPECT = 3E-15
 IDENTITIES = 61/194 (31%), POSITIVES = 89/194 (45%), GAPS = 26/194 (13%)

QUERY: 38  CGKKFCSRGSRCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97
          |   ||  |  | ++ | ||| | |+| |+|   |||||+|+ | |||+||| ||| | +
SBJCT: 29  CANVFCGAGRECAVTEK-GEPTCLCIEQCKPHKRPVCGSNGKTYLNHCELHRDACLTGSK 87

QUERY: 98  ITVIHSKDCFLKGDT--------CTMAGYARLKNVLLA-LQTRLQPLQEGDSRQDPASQK 148
          | | +   |  |            |  |    |+  |+  |+  + |    |       |
SBJCT: 88  IQVDYDGHCKEKKSASPSASPVVCYQANRDELRRRLIQWLEAEIIP----DGWFSKGSNY 143

QUERY: 149 RLLVESLFRDLDADGNGHLSSSELAQHVLKK-----------QDLDEDLLGCSPGDLLRF 197
            +++  |+  | +|+ || |||  + | +            |+ ++ |       |+
SBJCT: 144 SEILDKYFKSFD-NGDSHLDSSEFLKFVEQNETAINITTYADQENNKLLRSLCVDALIEL 202

QUERY: 198 DDYNSDSSLTLREF 211
           | |+|  |+ +||
SBJCT: 203 SDENADWKLSFQEF 216
```

The amino acid sequence of the FCTR2 protein has 63 of 193 amino acid residues (32%) identical to, and 89 of 193 residues (45%) positive with, the 299 amino acid residue protein Follastatin-Related Protein from the African Clawed Frog (GenBank Acc:JG0187) (SEQ ID NO:52) (Table 2I).

Table 2I. BLASTP of FCTR2 against Follastatin-Related Protein from the African Clawed Frog (SEQ ID NO:52)

```
>GI|7512162|PIR||JG0187 FOLLISTATIN-RELATED PROTEIN - AFRICAN CLAWED FROG
          LENGTH = 299

 SCORE = 81.8 BITS (201), EXPECT = 3E-14
 IDENTITIES = 63/193 (32%), POSITIVES = 89/193 (45%), GAPS = 25/193 (12%)

QUERY: 38  CGKKFCSRGSRCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97
          |   ||  |  | ++ | |+| | |+| |+    |||||+|+ | |||+||| ||| | +
SBJCT: 28  CANVFCGAGRECAVTEK-GDPTCDCIEKCKSHKRPVCGSNGKTYLNHCELHRDACLTGSK 86

QUERY: 98  ITVIHSKDCFLK-GDT-------CTMAGYARL-KNVLLALQTRLQPLQEGDSRQDPASQK 148
          | | +   |  |  ||       |  +    + + |+  ||| + `|    |       |
SBJCT: 87  IQVDYDGHCKEKTSDTPAAVPVACYQSDRDEMRRRVIHWLQTEITP----DGWFSKGSDY 142

QUERY: 149 RLLVESLFRDLDADGNGHLSSSELAQHVLKKQDL------DED----LLGCSPGDLLRFD 198
            +++  |+  | ||+ || |+||   + + |         ||+    |        |+
SBJCT: 143 SEILDRYFKKFD-DGDSHLDSAELQSFLEQSQSTNITTYKDEETNRMLKSLCVEALIELS 201

QUERY: 199 DYNSDSSLTLREF 211
           | |+|  |   ||
SBJCT: 202 DENADWKLNKNEF 214
```

The amino acid sequence of the FCTR2 protein has 59 of 194 amino acid residues (30%) identical to, and 90 of 194 residues (45%) positive with, the 308 amino acid residue protein Follistatin-Related Protein 1 Precursor from *Homo sapiens* (GenBank Acc:Q12841) (SEQ ID NO:53) (Table 2J).

Table 2J. BLASTP of FCTR2 against Follistatin-Related Protein 1 Precursor from *Homo sapiens* (SEQ ID NO:53)

```
>GI|5901956|REF|NP_009016.1| FOLLISTATIN-LIKE 1 [HOMO SAPIENS]
 GI|2498390|SP|Q12841|FRP_HUMAN FOLLISTATIN-RELATED PROTEIN 1 PRECURSOR
 GI|1082372|PIR||S51362 FOLLISTATIN-RELATED PROTEIN - HUMAN
 GI|536898|GB|AAA66062.1| (U06863) FOLLISTATIN-RELATED PROTEIN PRECURSOR [HOMO
SAPIENS]
 GI|3184393|DBJ|BAA28707.1| (D89937) FOLLISTATIN-RELATED PROTEIN (FRP) [HOMO SAPIENS]
 GI|12652619|GB|AAH00055.1|AAH00055 (BC000055) FOLLISTATIN-LIKE 1 [HOMO SAPIENS]
          LENGTH = 308

 SCORE = 82.9 BITS (204), EXPECT = 1E-14
 IDENTITIES = 59/194 (30%), POSITIVES = 90/194 (45%), GAPS = 26/194 (13%)

QUERY: 38  CGKKFCSRGSRCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97
           |   ||  |  | ++ | ||| | |+| |+|   |||||+|+ | |||+||| ||| | +
SBJCT: 31  CANVFCGAGRECAVTEK-GEPTCLCIEQCKPHKRPVCGSNGKTYLNHCELHRDACLTGSK 89

QUERY: 98  ITVIHSKDCFLKGD--------TCTMAGYARLKNVLLA-LQTRLQPLQEGDSRQDPASQK 148
           | | +   |  |           |  +    |+  ++  |+  + |    |       |
SBJCT: 90  IQVDYDGHCKEKKSVSPSASPVVCYQSNRDELRRRIIQWLEAEIIP----DGWFSKGSNY 145

QUERY: 149 RLLVESLFRDLDADGNGHLSSSELAQHVLKK-----------QDLDEDLLGCSPGDLLRF 197
             +++  |++ | +|+  | |||  + | +            |+ ++ | |      |+
SBJCT: 146 SEILDKYFKNFD-NGDSRLDSSEFLKFVEQNETAINITTYPDQENNKLLRGLCVDALIEL 204

QUERY: 198 DDYNSDSSLTLREF 211
           | |+|  |+ +||
SBJCT: 205 SDENADWKLSFQEF 218
```

The amino acid sequence of the FCTR2 protein has 35 of 69 amino acid residues (50%) identical to, and 45 of 69 residues (64%) positive with, the 315 amino acid residue Flik protein [*Gallus gallus*] (EMBL Acc:CAB42968.1) (SEQ ID NO:54) (Table 2K).

Table 2K. BLASTP of FCTR2 against Flik protein [*Gallus gallus*] (SEQ ID NO:54)

```
>GI|4837645|EMB|CAB42968.1| (AJ238977) FLIK PROTEIN [GALLUS GALLUS]
          LENGTH = 315

 SCORE = 79.8 BITS (196), EXPECT = 1E-13
 IDENTITIES = 35/69 (50%), POSITIVES = 45/69 (64%), GAPS = 1/69 (1%)

QUERY: 38  CGKKFCSRGSRCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97
           |   || ||+ | ++ | ||| | |+| |+|   |||||+|+ | |||+||| ||| | +
SBJCT: 31  CANVFCGRGAECAVTEK-GEPTCLCIEQCKPHGRPVCGSNGKTYLNHCELHRDACLTGSK 89

QUERY: 98  ITVIHSKDC 106
           | | +   |
SBJCT: 90  IQVDYDGHC 98
```

The amino acid sequence of the FCTR2 protein has 49 of 152 amino acid residues (32%) identical to, and 65 of 152 residues (42%) positive with a 272-420 amino acid fragment and, 31

of 83 residues (37%) identical to and 44 of 83 residues (52%) positive with a 248-329 amino acid fragment, both of the 1375 amino acid residue Frazzled gene protein [*Drosophila melanogaster*] (GenBankAcc:T13822) (SEQ ID NO:55) (Table 2L).

Table 2L. BLASTP of FCTR2 against Frazzled gene protein [*Drosophila melanogaster*] (SEQ ID NO:55)

```
>GI|7511861|PIR||T13822 FRAZZLED GENE PROTEIN - FRUIT FLY (DROSOPHILA MELANOGASTER)
 GI|1621115|GB|AAC47314.1| (U71001) FRAZZLED [DROSOPHILA MELANOGASTER]
          LENGTH = 1375

 SCORE = 69.4 BITS (169), EXPECT = 2E-10
 IDENTITIES = 49/152 (32%), POSITIVES = 65/152 (42%), GAPS = 4/152 (2%)

QUERY: 243 CAVHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGH-EQ 301
          |  +|  +| | | |||+ |+| ||+          || |+    |  ||| | ||   +
SBJCT: 272 CVANGVPKPQIKWLRNGMDLDFNDLDSRFSIVGTGSLQISSAEDIDSGNYQCRASNTVDS 331

QUERY: 302 LFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQ 361
          |     +||  ||      |+            |+|   | | | | |||||  ++     |
SBJCT: 332 LDAQATVQVQEPPKFIKAPKDTTAHEKDEPELKCDIWGKPKPVIRWLKNGDLITPNDYMQ 391

QUERY: 362 LSLLANGSELHISSVRYEDTGAYTCIAKNEVG 393
              | +|  | |  +   | | + |+  |  |
SBJCT: 392 ---LVDGHNLKILGLLNSDAGMFQCVGTNAAG 420

SCORE = 52.9 BITS (126), EXPECT = 1E-05
 IDENTITIES = 31/83 (37%), POSITIVES = 44/83 (52%), GAPS = 2/83 (2%)

QUERY: 311 NVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVS-TQMSKQLSLLANGS 369
          +| |   | |  +    |   +| | | |+| |+| ||+||+|+    +  + |++  ||
SBJCT: 248 SVAPSFLVGPSPKTVREGDTVTLDCVANGVPKPQIKWLRNGMDLDFNDLDSRFSIVGTGS 307

QUERY: 370 ELHISSVRYEDTGAYTCIAKNEV 392
            | |||    |+| | | | | |
SBJCT: 308 -LQISSAEDIDSGNYQCRASNTV 329
```

The amino acid sequence of the FCTR2 protein has 53 of 177 amino acid residues (29%) identical to, and 78 of 177 residues (43%) positive with a 366-539 amino acid fragment, 51 of 170 residues (30%) identical to and 74 of 170 residues (43%) positive with a 276-438 amino acid fragment, 46 of 165 amino acid residues (27%) identical to, and 74 of 165 amino acid residues positive with a 185-341 amino acid fragment, 48 of 167 amino acid residues (28%) identical to and 70 of 167 amino acid residues (41%) positive with a 77-243 amino acid fragment, and 28 of 84 amino acid residues (33%) and 37 of 84 amino acid residues positive with a 56-139 amino acid fragment all of the protein 1395 residue Roundabout 1 protein [*Drosophila melanogaster*] (GenBankAcc:AAC38849.1) (SEQ ID NO:56) (Table 2M).

Table 2M. BLASTP of FCTR2 against Roundabout 1 protein [*Drosophila melanogaster*] (SEQ ID NO:56)

```
>GI|2804782|GB|AAC38849.1| (AF040989) ROUNDABOUT 1 [DROSOPHILA MELANOGASTER]
          LENGTH = 1395

 SCORE = 69.8 BITS (170), EXPECT = 1E-10
 IDENTITIES = 53/177 (29%), POSITIVES = 78/177 (43%), GAPS = 11/177 (6%)
```

```
QUERY: 243 CAVHGDLRPP[redacted]RNGL-TLNFLDLEDINDF-GEDDSLYITKVTTI[redacted]NYTCHA---- 296
SBJCT: 366 CMASGNPPPSVFWTKEGVSTLMFPNSSHGRQYVAADGTLQITDVRQEDEGYYVCSAFSVV 425

QUERY: 297 --SGHEQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDV 354
SBJCT: 426 DSSTVRVFLQVSSVDERPPPIIQIGPANQTLPKGSVATLPCRATGNPSPRIKWFHDGHAV 485

QUERY: 355 STQMSKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVDEDISSLFIEDSARKTL 411
SBJCT: 486 --QAGNRYSII-QGSSLRVDDLQLSDSGTYTCTASGERGETSWAATLTVEKPGSTSL 539

SCORE = 56.3 BITS (135), EXPECT = 1E-06
 IDENTITIES = 51/170 (30%), POSITIVES = 74/170 (43%), GAPS = 12/170 (7%)

QUERY: 243 CAVHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGH-EQ 301
SBJCT: 276 CSVGGDPPPKVLWKKEEGNIPVSRARILHD---EKSLEISNITPTDEGTYVCEAHNNVGQ 332

QUERY: 302 LFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQM--- 358
SBJCT: 333 ISARASLIVHAPPNFTKRPSNKKVGLNGVVQLPCMASGNPPPSVFWTKEG--VSTLMFPN 390

QUERY: 359 -SKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVDEDISSLFIEDSA 407
SBJCT: 391 SSHGRQYVAADGTLQITDVRQEDEGYYVCSAFSV--VDSSTVRVFLQVSS 438

SCORE = 51.7 BITS (123), EXPECT = 3E-05
 IDENTITIES = 46/165 (27%), POSITIVES = 74/165 (43%), GAPS = 20/165 (12%)

QUERY: 251 PPIIWKRNGLTLNFLDLEDINDFG--------EDDSLYITKVTTIHMGNYTCHASG---- 298
SBJCT: 185 PTLIWIKDGVPLD--DLKAMS-FGASSRVRIVDGGNLLISNVEPIDEGNYKCIAQNLVGT 241

QUERY: 299 HEQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQM 358
SBJCT: 242 RESSYAKLIVQVK--PYFMKEPKDQVMLYGQTATFHCSVGGDPPPKVLWKKEEGNIPVSR 299

QUERY: 359 SKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVDEDISSLFI 403
SBJCT: 300 AR---ILHDEKSLEISNITPTDEGTYVCEAHNNVGQISARASLIV 341

SCORE = 44.0 BITS (103), EXPECT = 0.007
 IDENTITIES = 48/167 (28%), POSITIVES = 70/167 (41%), GAPS = 13/167 (7%)

QUERY: 243 CAVHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHM----GNYTCHASG 298
SBJCT: 77  CKVEGKPEPTIEWFKDGEPVSTNEKKSHRVQFKDGALFFYRTMQGKKEQDGGEYWCVAKN 136

QUERY: 299 H-EQLFQTHV-LQVNV-PPVIRVYPESQAQEPGVAASLRCH-AEGIPMPRITWLKNGVDV 354
SBJCT: 137 RVGQAVSRHASLQIAVLRDDFRVEPKDTRVAKGETALLECGPPKGIPEPTLIWIKDGVPL 196

QUERY: 355 STQMSKQLSL-----LANGSELHISSVRYEDTGAYTCIAKNEVGVDE 396
SBJCT: 197 DDLKAMSFGASSRVRIVDGGNLLISNVEPIDEGNYKCIAQNLVGTRE 243

SCORE = 42.9 BITS (100), EXPECT = 0.014
 IDENTITIES = 28/84 (33%), POSITIVES = 37/84 (43%), GAPS = 4/84 (4%)

QUERY: 314 PVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQLSLLANGSELH- 372
SBJCT: 56  PRIIEHPTDLVVKKNEPATLNCKVEGKPEPTIEWFKDGEPVSTNEKKSHRVQFKDGALFF 115

QUERY: 373 ---ISSVRYEDTGAYTCIAKNEVG 393
SBJCT: 116 YRTMQGKKEQDGGEYWCVAKNRVG 139
```

The amino acid sequence of the FCTR2 protein has 55 of 157 amino acid residues (35%) identical to, and [redacted] of 157 residues (47%) positive with a [redacted]-775 amino acid fragment, 49 of 163 residues (30%) identical to and 71 of 163 residues (43%) positive with a 335-492 amino acid fragment, 32 of 85 amino acid residues (37%) identical to, and 48 of 85 amino acid residues (55%) positive with a 1305-1388 amino acid fragment, 37 of 143 amino acid residues (25%) identical to and 60 of 143 amino acid residues (41%) positive with a 183-319 amino acid fragment, 43 of 174 amino acid residues (24%) and 70 of 174 amino acid residues (39%) positive with a 711-884 amino acid fragment, and 46 of 165 residues (27%) identical to and 69 of 165 residues positive with a 831-884 amino acid fragment all of the protein 1395 residue Down Syndrome Cell Adhesion Molecule Precursor (CHD2) from *Homo Sapiens* (GenBankAcc:O60469) (SEQ ID NO:57) (Table 2N).

Table 2N. BLASTP of FCTR2 against Down Syndrome Cell Adhesion Molecule Precursor (SEQ ID NO:57)

```
>gi|12643619|sp|O60469|DSCA_HUMAN DOWN SYNDROME CELL ADHESION MOLECULE PRECURSOR
(CHD2)
 GI|6740013|GB|AAF27525.1|AF217525_1 (AF217525) DOWN SYNDROME CELL ADHESION MOLECULE
[HOMO SAPIENS]
          LENGTH = 2012

 SCORE = 70.6 BITS (172), EXPECT = 6E-11
 IDENTITIES = 55/157 (35%), POSITIVES = 75/157 (47%), GAPS = 7/157 (4%)

QUERY: 245 VHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQLFQ 304
          | |||   | |+++|  +       |++     || |+ ++ +| ||||| |       +
SBJCT: 620 VSGDLPITITWQKDGRPIPGSLGVTIDNIDFTSSLRISNLSLMHNGNYTCIARNEAAAVE 679

QUERY: 305 THV-LQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITW-LKNGVDVST----QM 358
              | | |||   | |  |    | |  | | ||| |+| | |    |  |       +
SBJCT: 680 HQSQLIVRVPPKFVVQPRDQDGIYGKAVILNCSAEGYPVPTIVWKFSKGAGVPQFQPIAL 739

QUERY: 359 SKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVD 395
          + ++ +|+||| | |  |  ||+| | |   |+|| |
SBJCT: 740 NGRIQVLSNGS-LLIKHVVEEDSGYYLCKVSNDVGAD 775

SCORE = 50.6 BITS (120), EXPECT = 7E-05
 IDENTITIES = 49/163 (30%), POSITIVES = 71/163 (43%), GAPS = 16/163 (9%)

QUERY: 243 CAVHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQL 302
          |+| |     + | |||  ||       |     ++ | +  +     | | |     +
SBJCT: 335 CSVTGTEDQELSWYRNGEILNPGKNVRITGINHEN-LIMDHMVKSDGGAYQCFVRKDKLS 393

QUERY: 303 FQTH---VLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITW-------LKNGV 352
            | +   ||+   | +|  + | +   |     || |+ +| |+| |||       || |
SBJCT: 394 AQDYVQVVLEDGTPKIISAFSE-KVVSPAEPVSLMCNVKGTPLPTITWTLDDDPILKGG- 451

QUERY: 353 DVSTQMSKQLSLLAN-GSELHISSVRYEDTGAYTCIAKNEVGV 394
             | ++|+ ++   |  | |+||| +  | | | | | |  ||
SBJCT: 452 --SHRISQMITSEGNVVSYLNISSSQVRDGGVYRCTANNSAGV 492

SCORE = 47.9 BITS (113), EXPECT = 5E-04
 IDENTITIES = 32/85 (37%), POSITIVES = 48/85 (55%), GAPS = 6/85 (7%)

QUERY: 333  LRCHAEGIPMPRITWLK--NGVDVSTQMSKQLSLLANGSELHISSVRYEDTGAYTCIAKN 390
           | | | | | | + |+|  ||      +  + |+ +||| + | +|+ ||+| |+||| |
SBJCT: 1305 LPCKAVGDPSPAVKWMKDSNGTPSLVTIDGRRSIFSNGSFI-IRTVKAEDSGYYSCIANN 1363
```

```
QUERY: 391  EVGVDEDISSLFIE---DSARKTLA 412
           | || |  +    |  | |++
SBJCT: 1364 NWGSDEIIL  QVPPDQPRLTVS 1388

SCORE = 42.9 BITS (100), EXPECT = 0.015
 IDENTITIES = 37/143 (25%), POSITIVES = 60/143 (41%), GAPS = 6/143 (4%)

QUERY: 270 INDFGEDDSLYITKVTTIHMGNYTCHASGHEQLFQTHVLQVNVPPVIRVYPESQAQEPGV 329
          | |   +| ||  +  | |         |   +|| +     |  | |    + +    |
SBJCT: 183 IKDVQNEDGLYNYRCITRHRYTGETRQSNSARLFVSD--PANSAPSILDGFDHRKAMAGQ 240

QUERY: 330 AASLRCHAEGIPMPRITWLKNGVDVSTQMSKQLSLLANGSELHISSVRYEDTGAYTCIAK 389
              | | | | | |   |||+  ++  ++| +      |  | | ++|  |+|+| |
SBJCT: 241 RVELPCKALGHPEPDYRWLKD--NMPLELSGRFQKTVTG--LLIENIRPSDSGSYVCEVS 296

QUERY: 390 NEVGVDEDISSLFIEDSARKTLA 412
          |  |  + |  |+++   + |++
SBJCT: 297 NRYGTAKVIGRLYVKQPLKATIS 319

 SCORE = 41.3 BITS (96), EXPECT = 0.047
 IDENTITIES = 43/174 (24%), POSITIVES = 70/174 (39%), GAPS = 11/174 (6%)

QUERY: 243 CAVHGDLRPPIIWK--RNGLTLNF--LDLEDINDFGEDDSLYITKVTTIHMGNYTCHASG 298
          |+  |   | |+||  +      |  + |        + || |  |     | | |  |
SBJCT: 711 CSAEGYPVPTIVWKFSKGAGVPQFQPIALNGRIQVLSNGSLLIKHVVEEDSGYYLCKVSN 770

QUERY: 299 H--EQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVST 356
               + ++  | | +| +|  || +     |    + | | |     + | |    ++
SBJCT: 771 DVGADVSKSMYLTVKIPAMITSYPNTTLATQGQKKEMSCTAHGEKPIIVRWEKEDRIINP 830

QUERY: 357 QMSKQLSLLANGSELHISSVRY-----EDTGAYTCIAKNEVGVDEDISSLFIED 405
          +|++ |       |  ||+++      ||+| ++| | |  | |  |  | +++
SBJCT: 831 EMARYLVSTKEVGEEVISTLQILPTVREDSGFFSCHAINSYGEDRGIIQLTVQE 884

SCORE = 40.6 BITS (94), EXPECT = 0.074
 IDENTITIES = 46/165 (27%), POSITIVES = 69/165 (40%), GAPS = 7/165 (4%)

QUERY: 243 CAVHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTT-IHMGNYTCHASGHEQ 301
          | | |      | | +|   | |   +    |  + +| ++ |   +  | |||+     |
SBJCT: 525 CRVIGYPYYSIKWYKNSNLLPFNHRQVA--FENNGTLKLSDVQKEVDEGEYTCNVLVQPQ 582

QUERY: 302 LFQTHVLQVN--VPPVIRVYPESQAQEPGVAASLRCHAEGIPMP-RITWLKNGVDVSTQM 358
          |  +  + |   ||| |+ + |       |    + |       +|  ||| |+|  +   +
SBJCT: 583 LSTSQSVHVTVKVPPFIQPF-EFPRFSIGQRVFIPCVVVSGDLPITITWQKDGRPIPGSL 641

QUERY: 359 SKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVDEDISSLFI 403
             +  +   | | ||++     | |||||+||    |  | | +
SBJCT: 642 GVTIDNIDFTSSLRISNLSLMHNGNYTCIARNEAAAVEHQSQLIV 686
```

The amino acid sequence of the FCTR2 protein has 55 of 194 amino acid residues (28%) identical to, and 86 of 194 residues (44%) positive with Limbic System-Associated Membrane Protein Precursor (LSAMP) from *Homo sapiens* (SWISSPROT Acc:Q13449) (SEQ ID NO:58) (Table 2O).

Table 2O. BLASTP of FCTR2 against Limbic System-Associated Membrane Protein Precursor (SEQ ID NO:58)

```
PTNR:SWISSPROT-ACC:Q13449 LIMBIC SYSTEM-ASSOCIATED MEMBRANE PROTEIN PRECURSOR
(LSAMP) - HOMO SAPIENS (HUMAN), 338 AA.

           LENGTH = 338

 SCORE = 191 (67.2 BITS), EXPECT = 6.7E-12, P = 6.7E-12
 IDENTITIES = 55/194 (28%), POSITIVES = 86/194 (44%)
```

The amino acid sequence of the FCTR2 protein has 68 of 190 amino acid residues (35%) identical to, and 92 of 190 residues (48%) positive with Putative Neuronal Cell Adhesion Molecule, Short Form from *Mus musculus* (SPTREMBL Acc:O70246) (SEQ ID NO:59) (Table 2P).

Table 2P. BLASTP of FCTR2 against Putative Neuronal Cell Adhesion Molecule, Short Form from *Mus musculus* (SEQ ID NO:59)

```
PTNR:SPTREMBL-ACC:O70246 PUTATIVE NEURONAL CELL ADHESION MOLECULE (PUNC)
(PUTATIVE NEURONAL CELL ADHESION MOLECULE, SHORT FORM) - MUS MUSCULUS
(MOUSE), 793 AA
          LENGTH = 793

 SCORE = 203 (71.5 BITS), EXPECT = 7.0E-12, SUM P(2) = 7.0E-12
 IDENTITIES = 68/190 (35%), POSITIVES = 92/190 (48%)
```

The amino acid sequence of the FCTR2 protein has 58 of 199 amino acid residues (29%) identical to, and 91 of 199 residues (45%) positive with CHLAMP, G11-Isoform Precursor from *Gallus gallus* (SPTREMBL Acc: O02869) (SEQ ID NO:60) (Table 2Q).

Table 2Q. BLASTP of FCTR2 against CHLAMP, G11-Isoform Precursor from *Gallus gallus* (SEQ ID NO:60)

```
PTNR:SPTREMBL-ACC:O02869 CHLAMP, G11-ISOFORM PRECURSOR - GALLUS GALLUS
(CHICKEN), 350 AA.
          LENGTH = 350

 SCORE = 191 (67.2 BITS), EXPECT = 7.7E-12, P = 7.7E-12
 IDENTITIES = 58/199 (29%), POSITIVES = 91/199 (45%)
```

The amino acid sequence of the FCTR2 protein has 55 of 194 amino acid residues (28%) identical to, and 86 of 194 residues (44%) positive with Limbic System-Associated Membrane Protein Precursor (LSAMP) from *Rattus norvegicus* (SWISSPROT Acc:Q62813) (SEQ ID NO:61) (Table 2R).

Table 2R. BLASTP of FCTR2 against Limbic System-Associated Membrane Protein Precursor (LSAMP) from *Rattus norvegicus* (SEQ ID NO:61)

```
PTNR:SWISSPROT-ACC:Q62813 LIMBIC SYSTEM-ASSOCIATED MEMBRANE PROTEIN PRECURSOR
(LSAMP) - RATTUS NORVEGICUS (RAT), 338 AA.
          LENGTH = 338

 SCORE = 188 (66.2 BITS), EXPECT = 1.5E-11, P = 1.5E-11
 IDENTITIES = 55/194 (28%), POSITIVES = 86/194 (44%)
```

FCTR2 protein has similarity to cell adhesion molecules, follistatin, roundabout and frazzled (see BlastP results). These genes are involved in neuronal development and

reproductive physiology. Frazzled encodes a Drosophila member of the DCC immunoglobulin subfamily and is required for CNS and motor axon guidance (Cell 87:197-204(1996)). Characterization of a rat C6 glioma-secreted follistatin-related protein (FRP) and cloning and sequence of the human homologue is described in Eur. J. Biochem. 225:937-946(1994). This protein may modulate the action of some growth factors on cell proliferation and differentiation. FRP binds heparin. The follistatin-related protein is a secreted protein and has one follistatin-like domain. The cloning and early dorsal axial expression of Flik, a chick follistatin-related gene and evidence for involvement in dorsalization/neural induction is presented in Dev. Biol. 178:327-342(1996). Roundabout controls axon crossing of the CNS midline and defines a novel subfamily of evolutionarily conserved guidance receptors, as shown in Cell 92:205-215(1998). cDNA cloning and structural analysis of the human limbic-system- associated membrane protein (LAMP) is described in Gene 170:189-195(1996). LAMP, a protein of the OBCAM family that contains three immunoglobulin-like C2-type domains, mediates selective neuronal growth and axon targeting. LAMP contributes to the guidance of developing axons and remodeling of mature circuits in the limbic system. This protein is essential for normal growth of the hippocampal mossy fiber projection. LAMP is attached to the membrane by a GPI-Anchor. It is expressed on limbic neurons and fiber tracts as well as in single layers of the superior colliculus, spinal chord and cerbellum. Characterization of the human full-length PTK7 cDNA encoding a receptor protein tyrosine kinase-like molecule closely related to chick KLG is disclosed in J. Biochem. 119:235-239(1996). Based upon homology, FCTR2 proteins and each homologous protein or peptide may share at least some activity.

Functions and therapeutic uses:

The OMIM gene map has identified this region which the invention maps to (5q21-5q31) as associated with susceptibility to the following diseases (OMIM Ids are underlined):

- Allergy and asthma
- Hemangioma,
- capillary infantile Schistosoma mansoni infection, susceptibility/resistance to Spinocerebellar ataxia
- Bronchial asthma
- Plasmodium falciparum parasitemia,
- intensity of Corneal dystrophy, Groenouw type I, 121900; Corneal dystrophy,lattice type I, 122200;
- Reis-Bucklers corneal dystrophy;Corneal dystrophy, Avellino type Eosinophilia, familial Myelodysplastic syndrome;

- Myelogenous leukemia, Acute Cutis laxa, recessive, type I, Deafness, autosomal dominant nonsyndromic sensorineural, 1 Contractural arachnodactyly, Congenital Neonatal alloimmune thrombocytopenia;
- Glycoprotein Ia deficiency Male infertility;
- Charcot-Marie-Tooth neuropathy, Demyelinating Gardner syndrome ;
- Adenomatous polyposis coli;
- Colorectal cancer;
- Desmoid disease, hereditary, 135290;
- Turcot syndrome,276300;
- Adenomatous polyposis coli, attenuated
- Colorectal cancer

Therefore the invention is implicated in at least all of the above mentioned diseases and may have therapeutic uses for these diseases.

This sequence has similarity to cell adhesion molecules, follistatin, roundabout and frazzled (see BlastP results). These genes are involved in neuronal development and reproductive physiology. Therefore the invention is also implicated in disorders such as or therapeutic uses for:

- Neurodegenerative disorders, nerve trauma, epilepsy, mental health conditions
- Tissue regeneration in vivo and in vitro

Female reproductive system disorders and pregnancy

FCTR3

FCTR3, is an amino acid type II membrane, neurestin-like protein. The FCTR3a nucleic acid of 1430 nucleotides (also designated 10129612.0.118) is shown in Table 3A. An ORF was identified beginning with an ATG initiation codon at nucleotides 69-71 and ending with a TAG codon at nucleotides 1212-1214. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 3A, and the start and stop codons are in bold letters.

Table 3A. FCTR3a Nucleotide Sequence (SEQ ID NO:5)

AAAAAAGGCGGGGGGTGGACTTAGCAGTGTAATTTGAGACCGGTGGTAAGGATTGGAGCGAGCTAGAGATGCTGCACGCTGCTAACA
AGGGAAGGAAGCCTTCAGCTGAGGCAGGTCGTCCCATTCCACCTACATCCTCGCCTAGTCTCCTCCCATCTGCTCAGCTGCCTAGCT
CCCATAATCCTCCACCAGTTAGCTGCCAGATGCCATTGCTAGACAGCAACACCTCCCATCAAATCATGGACACCAACCCTGATGAGG
AATTCTCCCCCAATTCATACCTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCGAACCACCACAGCCAGT
CGACTCTGAGGCCCCCTCTCCCACCCCCTCACAACCACACGCTGTCCCATCACCACTCGTCCGCCAACTCCCTCAACAGGAACTCAC
TGACCAATCGGCGGAGTCAGATCCACGCCCCGGCCCCAGCGCCCAATGACCTGGCCACCACACCAGAGTCCGTTCAGCTTCAGGACA
GCTGGGTGCTAAACAGCAACGTGCCACTGGAGACCCGGCACTTCCTCTTCAAGACCTCCTCGGGGAGCACACCCTTGTTCAGCAGCT

CTTCCCCGGGATACCCTTTGACCTCAGGAACGGTTTACACGCCCCCGCCCCGCCTGCTGCCCAGGAATACTTTCTCCAGGAAGGCTT
TCAAGCTGAAGAAGCCCTCCA[redacted]CTGCAGCTGGAAATGTGCTGCCCTCTCCGCCA[redacted]CGCGGCCCTCCTCTTGGCTATTTTGC
TGGCGTATTTCATAGTGCCCT[redacted]GTTGAAAAACAGCAGCATAGACAGTGGTGAAG[redacted]AGTTGGTCGGCGGGTAACACAAGAAG
TCCCACCAGGGGTGTTTTGGAGGTCACAAATTCACATCAGTCAGCCCCAGTTCTTAAAGTTCAACATCTCCCTCGGGAAGGACGCTC
TCTTTGGTGTTTACATAAGAAGAGGACTTCCACCATCTCATGCCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGAGAAGTGGA
GTGTGGTTGAGTCTCCCAGGGAACGCCGGAGCATACAGACCTTGGTTCAGAATGAAGCCGTGTTTGTGCAGTACCTGGATGTGGGCC
TGTGGCATCTGGCCTTCTACAATGATGGAAAAGACAAAGAGATGGTTTCCTTCAATACTGTTGTCCTAGATGGGACCATCTAGTTGC
AGAAAAACAAGCTCAGGGCGCCCACTGATTTGACATTATGATTCAGTGCAGGACTGTCCACGTAACTGCCATGGGAATGGTGAATGT
GTGTCCGGGGTGTGTCACTGTTTCCCAGGATTTCTAGGAGCAGACTGTGCTAAAGACCTTCCTGCCTTGACTTTCTGCAAGACAATC
ATTAATAAAGCTGCTCTGTAAATACTAAAAAAAAAACA

The FCTR3 polypeptide (SEQ ID NO:5) encoded by SEQ ID NO:5 is 381 amino acid residues and is presented using the one-letter code in Table 3B.

Table 3B. Encoded FCTR3a protein sequence (SEQ ID NO:6).

MLHAANKGRKPSAEAGRPIPPTSSPSLLPSAQLPSSHNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGP
PNHHSQSTLRPPLPPPHNHTLSHHHSSANSLNRNSLTNRRSQIHAPAPAPNDLATTPESVQLQDSWVLNSNVPLETRHFLFKTSSGS
TPLFSSSSPGYPLTSGTVYTPPPRLLPRNTFSRKAFKLKKPSKYCSWKCAALSAIAAALLLAILLAYFIVPWSLKNSSIDSGEAEVG
RRVTQEVPPGVFWRSQIHISQPQFLKFNISLGKDALFGVYIRRGLPPSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVFV
QYLDVGLWHLAFYNDGKDKEMVSFNTVVLDGTI

In an alternative embodiment, the 5' end of the FCTR3a nucleic acid could be extended as it is in the 9826bp FCTR3b (also referred to herein as 10129612.0.405) shown in Table 3C. An ORF was identified beginning with an ATG initiation codon at nucleotides 280-282 and ending with a TAA codon at nucleotides 8479-8481. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 3C, and the start and stop codons are in bold letters. Italicized bases 1-201 refer to a variable 5' region that will be further discussed below.

Table 3C. FCTR3b Nucleotide Sequence (SEQ ID NO:7)

TTTAAATCCTCATACCTTAAAGGAGATGTGTATATAAGGGAGTTGGAACCAGCATTAGATGAGTTGACAAAAATGCAGTT
TCAGTTCTAGAGGTCTGGGAAGTCCAAGAACAAGGTGCTGGCAGATTGGATTCCCCGTGAGGGCTTTCTTCCTGGCTTGA
*AGTTGGCTGCTTTCCTGCTGAGACTTCTCATGGCAGAGACTGAG*GGTGGCAAAGTGACAAGTGCCAAAACTCAGGCCTGA
CTTTTCTGAAAACATCAGCATTCTGCCATATCTGGAATA**ATG**GATGTAAAGGACCGGCGACACCGCTCTTTGACCAGAGG
ACGCTGTGGCAAAGAGTGTCGCTACACAAGCTCCTCTCTGGACAGTGAGGACTGCCGGGTGCCCACACAGAAATCCTACA
GCTCCAGTGAGACTCTGAAGGCCTATGACCATGACAGCAGGATGCACTATGGAAACCGAGTCACAGACCTCATCCACCGG
GAGTCAGATGAGTTTCCTAGACAAGGAACCAACTTCACCCTTGCCGAACTGGGCATCTGTGAGCCCTCCCCACACCGAAG
CGGCTACTGCTCCGACATGGGGATCCTTCACCAGGGCTACTCCCTTAGCACAGGGTCTGACGCCGACTCCGACACCGAGG
GAGGGATGTCTCCAGAACACGCCATCAGACTGTGGGGCAGAGGGATAAAATCCAGGCGCAGTTCCGGCCTGTCCAGTCGT
GAAAACTCGGCCCTTACCCTGACTGACTCTGACAACGAAAACAAATCAGATGATGAGAACGGTCGTCCCATTCCACCTAC
ATCCTCGCCTAGTCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATAATCCTCCACCAGTTAGCTGCCAGATGCCATTGC
TAGACAGCAACACCTCCCATCAAATCATGGACACCAACCCTGATGAGGAATTCTCCCCCAATTCATACCTGCTCAGAGCA
TGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCGAACCACCACAGCCAGTCGACTCTGAGGCCCCCTCTCCCACC
CCCTCACAACCACACGCTGTCCCATCACCACTCGTCCGCCAACTCCCTCAACAGGAACTCACTGACCAATCGGCGGAGTC
AGATCCACGCCCCGGCCCCAGCGCCCAATGACCTGGCCACCACACCAGAGTCCGTTCAGCTTCAGGACAGCTGGGTGCTA
AACAGCAACGTGCCACTGGAGACCCGGCACTTCCTCTTCAAGACCTCCTCGGGGAGCACACCCTTGTTCAGCAGCTCTTC
CCCGGGATACCCTTTGACCTCAGGAACGGTTTACACGCCCCCGCCCCGCCTGCTGCCCAGGAATACTTTCTCCAGGAAGG
CTTTCAAGCTGAAGAAGCCCTCCAAATACTGCAGCTGGAAATGTGCTGCCCTCTCCGCCATTGCCGCGGCCCTCCTCTTG
GCTATTTTGCTGGCGTATTTCATAGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCG
GCGGGTAACACAAGAAGTCCCACCAGGGGTGTTTTGGAGGTCACAAATTCACATCAGTCAGCCCCAGTTCTTAAAGTTCA
ACATCTCCCTCGGGAAGGACGCTCTCTTTGGTGTTTACATAAGAAGAGGACTTCCACCATCTCATGCCCAGTATGACTTC
ATGGAACGTCTGGACGGGAAGGAGAAGTGGAGTGTGGTTGAGTCTCCCAGGGAACGCCGGAGCATACAGACCTTGGTTCA
GAATGAAGCCGTGTTTGTGCAGTACCTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGATGGAAAAGACAAAGAGA
TGGTTTCCTTCAATACTGTTGTCCTAGATTCAGTGCAGGACTGTCCACGTAACTGCCATGGGAATGGTGAATGTGTGTCC
GGGGTGTGTCACTGTTTCCCAGGATTTCTAGGAGCAGACTGTGCTAAAGCTGCCTGCCCTGTCCTGTGCAGTGGGAATGG
ACAATATTCTAAAGGGACGTGCCAGTGCTACAGCGGCTGGAAAGGTGCAGAGTGCGACGTGCCCATGAATCAGTGCATCG
ATCCTTCCTGCGGGGGCCACGGCTCCTGCATTGATGGGAACTGTGTCTGCTCTGCTGGCTACAAAGGCGAGCACTGTGAG

GAAGTTGATTGCTTGGATCCCACCTGCTCCAGCCACGGAGTCTGTGTGAATGGAGAATGCCTGTGCAGCCCTGGCTGGGG
TGGTCTGAACTGTGAGCTGGC[redacted]GTCCAGTGCCCAGACCAGTGCAGTGGGCATGG[redacted]TACCTGCCTGACACGGGCC
TCTGCAGCTGCGATCCCAACT[redacted]GGGTCCCGACTGCTCTGTTGAAGTGTGCTCAGT[redacted]CTGTGGCACTCACGGCGTC
TGCATCGGGGGAGCCTGCCGCTGTGAAGAGGGCTGGACAGGCGCAGCGTGTGACCAGCGCGTGTGCCACCCCCGCTGCAT
TGAGCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTGCACCATTGGTAGGCAAA
CGGCAGGCACCGAAACAGATGGCTGCCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGTCAGAACAGCTGGCAG
TGTGTCTGCCAGACCGGCTGGAGAGGGCCCGGATGCAACGTTGCCATGGAAACTTCCTGTGCTGATAACAAGGATAATGA
GGGAGATGGCCTGGTGGATTGTTTGGACCCTGACTGCTGCCTGCAGTCAGCCTGTCAGAACAGCCTGCTCTGCCGGGGGT
CCCGGGACCCACTGGACATCATTCAGCAGGGCCAGACGGATTGGCCCGCAGTGAAGTCCTTCTATGACCGTATCAAGCTC
TTGGCAGGCAAGGATAGCACCCACATCATTCCTGGAGAGAACCCTTTCAACAGCAGCTTGGTTTCTCTCATCCGAGGCCA
AGTAGTAACTACAGATGGAACTCCCCTGGTCGGTGTGAACGTGTCTTTTGTCAAGTACCCAAAATACGGCTACACCATCA
CCCGCCAGGATGGCACGTTCGACCTGATCGCAAATGGAGGTGCTTCCTTGACTCTACACTTTGAGCGAGCCCCGTTCATG
AGCCAGGAGCGCACTGTGTGGCTGCCGTGGAACAGCTTTTACGCCATGGACACCCTGGTGATGAAGACCGAGGAGAACTC
CATCCCCAGCTGTGACCTCAGTGGCTTTGTCCGGCCTGATCCAATCATCATCTCCTCCCCACTGTCCACCTTCTTTAGTG
CTGCCCCTGGGCAGAATCCCATCGTGCCTGAGACCCAGGTTCTTCATGAAGAAATCGAGCTCCCTGGTTCCAATGTGAAA
CTTCGCTATCTGAGCTCTAGAACTGCAGGGTACAAGTCACTGCTGAAGATCACCATGACCCAGTCCACAGTGCCCCTGAA
CCTCATTAGGGTTCACCTGATGGTGGCTGTCGAGGGGCATCTCTTCCAGAAGTCATTCCAGGCTTCTCCCAACCTGGCCT
CCACCTTCATCTGGGACAAGACAGATGCGTATGGCCAAAGGGTGTATGGACTCTCAGATGCTGTTGTGTCTGTCGGGTTT
GAATATGAGACCTGTCCCAGTCTAATTCTCTGGGAGAAAAGGACAGCCCTCCTTCAGGGATTCGAGCTGGACCCCTCCAA
CCTCGGTGGCTGGTCCCTAGACAAACACCACATCCTCAATGTTAAAAGTGGAATCCTACACAAAGGCACTGGGGAAAACC
AGTTCCTGACCCAGCAGCCTGCCATCATCACCAGCATCATGGGCAATGGTCGCCGCCGGAGCATTTCCTGTCCCAGCTGC
AACGGCCTTGCTGAAGGCAACAAGCTGCTGGCCCCAGTGGCTCTGGCTGTTGGAATCGATGGGAGCCTCTATGTGGGTGA
CTTCAATTACATCCGACGCATCTTTCCCTCTCGAAATGTGACCAGCATCTTGGAGTTACGAAATAAAGAGTTTAAACATA
GCAACAACCCAGCACACAAGTACTACTTGGCAGTGGACCCCGTGTCCGGCTCGCTCTACGTGTCCGACACCAACAGCAGG
AGAATCTACCGCGTCAAGTCTCTGAGTGGAACCAAAGACCTGGCTGGGAATTCGGAAGTTGTGGCAGGGACGGGAGAGCA
GTGTCTACCCTTTGATGAAGCCCGCTGCGGGGATGGAGGGAAGGCCATAGATGCAACCCTGATGAGCCCGAGAGGTATTG
CAGTAGACAAGAATGGGCTCATGTACTTTGTCGATGCCACCATGATCCGGAAGGTTGACCAGAATGGAATCATCTCCACC
CTGCTGGGCTCCAATGACCTCACTGCCGTCCGGCCGCTGAGCTGTGATTCCAGCATGGATGTAGCCCAGGTTCGTCTGGA
GTGGCCAACAGACCTTGCTGTCAATCCCATGGATAACTCCTTGTATGTTCTAGAGAACAATGTCATCCTTCGAATCACCG
AGAACCACCAAGTCAGCATCATTGCGGGACGCCCCATGCACTGCCAAGTTCCTGGCATTGACTACTCACTCAGCAAACTA
GCCATTCACTCTGCCCTGGAGTCAGCCAGTGCCATTGCCATTTCTCACACTGGGGTCCTCTACATCACTGAGACAGATGA
GAAGAAGATTAACCGTCTACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCGACT
GCAAAAACGATGTCAATTGCAACTGCTATTCAGGAGATGATGCCTACGCGACTGATGCCATCTTGAATTCCCCATCATCC
TTAGCTGTAGCTCCAGATGGTACCATTTACATTGCAGACCTTGGAAATATTCGGATCAGGGCGGTCAGCAAGAACAAGCC
TGTTCTTAATGCCTTCAACCAGTATGAGGCTGCATCCCCCGGAGAGCAGGAGTTATATGTTTTCAACGCTGATGGCATCC
ACCAATACACTGTGAGCCTGGTGACAGGGGAGTACTTGTACAATTTCACATATAGTACTGACAATGATGTCACTGAATTG
ATTGACAATAATGGGAATTCCCTGAAGATCCGTCGGGACAGCAGTGGCATGCCCCGTCACCTGCTCATGCCTGACAACCA
GATCATCACCCTCACCGTGGGCACCAATGGAGGCCTCAAAGTCGTGTCCACACAGAACCTGGAGCTTGGTCTCATGACCT
ATGATGGCAACACTGGGCTCCTGGCCACCAAGAGCGATGAAACAGGATGGACGACTTTCTATGACTATGACCACGAAGGC
CGCCTGACCAACGTGACGCGCCCCACGGGGGTGGTAACCAGTCTGCACCGGGAAATGGAGAAATCTATTACCATTGACAT
TGAGAACTCCAACCGTGATGATGACGTCACTGTCATCACCAACCTCTCTTCAGTAGAGGCCTCCTACACAGTGGTACAAG
ATCAAGTTCGGAACAGCTACCAGCTCTGTAATAATGGTACCCTGAGGGTGATGTATGCTAATGGGATGGGTATCAGCTTC
CACAGCGAGCCCCATGTCCTAGCGGGCACCATCACCCCCACCATTGGACGCTGCAACATCTCCCTGCCTATGGAGAATGG
CTTAAACTCCATTGAGTGGCGCCTAAGAAAGGAACAGATTAAAGGCAAAGTCACCATCTTTGGCAGGAAGCTCCGGGTCC
ATGGAAGAAATCTCTTGTCCATTGACTATGATCGAAATATTCGGACTGAAAAGATCTATGATGACCACCGGAAGTTCACC
CTGAGGATCATTTATGACCAGGTGGGCCGCCCCTTCCTCTGGCTGCCCAGCAGCGGGCTGGCAGCTGTCAACGTGTCATA
CTTCTTCAATGGGCGCCTGGCTGGGCTTCAGCGTGGGGCCATGAGCGAGAGGACAGACATCGACAAGCAAGGCCGCATCG
TGTCCCGCATGTTCGCTGACGGGAAAGTGTGGAGCTACTCCTACCTTGACAAGTCCATGGTCCTCCTGCTTCAGAGCCAA
CGTCAGTATATATTTGAGTATGACTCCTCTGACCGCCTCCTTGCCGTCACCATGCCCAGCGTGGCCCGGCACAGCATGTC
CACACACACCTCCATCGGCTACATCCGTAATATTTACAACCCGCCTGAAAGCAATGCTTCGGTCATCTTTGACTACAGTG
ATGACGGCCGCATCCTGAAGACCTCCTTTTTGGGCACCGGACGCCAGGTGTTCTACAAGTATGGGAAACTCTCCAAGTTA
TCAGAGATTGTCTACGACAGTACCGCCGTCACCTTCGGGTATGACGAGACCACTGGTGTCTTGAAGATGGTCAACCTCCA
AAGTGGGGGCTTCTCCTGCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTACAGGTTCTCCGAGG
AAGGCATGGTCAATGCCAGGTTTGACTACACCTATCATGACAACAGCTTCCGCATCGCAAGCATCAAGCCCGTCATAAGT
GAGACTCCCCTCCCCGTTGACCTCTACCGCTATGATGAGATTTCTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCAT
CTATTATGACATCAACCAGATCATCACCACTGCCGTGATGACCCTCAGCAAACACTTCGACACCCATGGGCGGATCAAGG
AGGTCCAGTATGAGATGTTCCGGTCCCTCATGTACTGGATGACGGTGCAATATGACAGCATGGGCAGGGTGATCAAGAGG
GAGCTAAAACTGGGGCCCTATGCCAATACCACGAAGTACACCTATGACTACGATGGGGACGGGCAGCTCCAGAGCGTGGC
CGTCAATGACCGCCCGACCTGGCGCTACAGCTATGACCTTAATGGGAATCTCCACTTACTGAACCCAGGCAACAGTGTGC
GCCTCATGCCCTTGCGCTATGACCTCCGGGATCGGATAACCAGACTCGGGGATGTGCAGTACAAAATTGACGACGATGGC
TATCTGTGCCAGAGAGGGTCTGACATCTTCGAATACAATTCCAAGGGCCTCCTAACAAGAGCCTACAACAAGGCCAGCGG
GTGGAGTGTCCAGTACCGCTATGATGGCGTAGGACGGCGGGCTTCCTACAAGACCAACCTGGGCCACCACCTGCAGTACT
TCTACTCTGACCTCCACAACCCGACGCGCATCACCCATGTCTACAATCACTCCAACTCGGAGATTACCTCACTGTACTAC
GACCTCCAGGGCCACCTCTTTGCCATGGAGAGCAGCAGTGGGGAGGAGTACTATGTTGCCTCTGATAACACAGGGACTCC
TCTGGCTGTGTTCAGCATCAACGGCCTCATGATCAAACAGCTGCAGTACACGGCCTATGGGGAGATTTATTATGACTCCA
ACCCCGACTTCCAGATGGTCATTGGCTTCCATGGGGGACTCTATGACCCCCTGACCAAGCTGGTCCACTTCACTCAGCGT
GATTATGATGTGCTGGCAGGACGATGGACCTCCCCAGACTATACCATGTGGAAAAACGTGGGCAAGGAGCCGGCCCCCTT
TAACCTGTATATGTTCAAGAGCAACAATCCTCTCAGCAGTGAGCTAGATTTGAAGAACTACGTGACAGATGTGAAAAGCT
GGCTTGTGATGTTTGGATTTCAGCTTAGCAACATCATTCCTGGCTTCCCGAGAGCCAAAATGTATTTCGTGCCTCCTCCC
TATGAATTGTCAGAGAGTCAAGCAAGTGAGAATGGACAGCTCATTACAGGTGTCCAACAGACAACAGAGAGACATAACCA

GGCCTTCATGGCTCTGGAAGGACAGGTCATTACTAAAAAGCTCCACGCCAGCATCCGAGAGAAAGCAGGTCACTGGTTTG
CCACCACCACGCCCATCATTG[redacted]AGGCATCATGTTTGCCATCAAAGAAGGGCGGG[redacted]CACGGGCGTGTCCAGCATC
GCCAGCGAAGATAGCCGCAAG[redacted]CATCTGTGCTGAACAACGCCTACTACCTGGAC[redacted]TGCACTACAGCATCGAGGG
CAAGGACACCCACTACTTTGTGAAGATTGGCTCAGCCGATGGCGACCTGGTCACACTAGGCACCACCATCGGCCGCAAGG
TGCTAGAGAGCGGGGTGAACGTGACCGTGTCCCAGCCCACGCTGCTGGTCAACGGCAGGACTCGAAGGTTCACGAACATT
GAGTTCCAGTACTCCACGCTGCTGCTCAGCATCCGCTATGGCCTCACCCCCGACACCCTGGACGAAGAGAAGGCCCGCGT
CCTGGACCAGGCGAGACAGAGGGCCCTGGGCACGGCCTGGGCCAAGGAGCAGCAGAAAGCCAGGGACGGGAGAGAGGGGA
GCCGCCTGTGGACTGAGGGCGAGAAGCAGCAGCTTCTGAGCACCGGGCGCGTGCAAGGGTACGAGGGATATTACGTGCTT
CCCGTGGAGCAATACCCAGAGCTTGCAGACAGTAGCAGCAACATCCAGTTTTTAAGACAGAATGAGATGGGAAAGAGGTA
ACAAAATAATCTGCTGCCATTCCTTGTCTGAATGGCTCAGCAGGAGTAACTGTTATCTCCTCTCCTAAGGAGATGAAGAC
CTAACAGGGGCACTGCGGCTGGGCTGCTTTAGGAGACCAAGTGGCAAGAAAGCTCACATTTTTTGAGTTCAAATGCTACT
GTCCAAGCGAGAAGTCCCTCATCCTGAAGTAGACTAAAGCCCGGCTGAAAATTCCGAGGAAAACAAAACAAACGAATGAA
TGAACAGACACACACAATGTTCCAAGTTCCCCTAAAATATGACCCACTTGTTCTGGGTCTACGCAGAAAAGAGACGCAAA
GTGTCCAAAAGGAACAAAAGAACAAAAACGAATAAGCAAAGAAGAAAACAAACAAAAACAAAACAAAACAAACACACGGA
CCGATAAACAAAGAAGCGAAGATAAGAAAGAAGGCCTCATATCCAATTACCTCACTCATTCACATGTGAGCGACACGCAG
ACATCCGCGAGGGCCAGCGTCACCAGACCAGCTGCGGGACAAACCACTCAGACTGCTTGTAGGACAAATACTTCTGACAT
TTTCGTTTAAGCAAATACAGGTGCATTTAAAACACGACTTTGGGGGTGATTTGTGTGTAGCGCCTGGGGAGGGGGGATAA
AAGAGGAGGAGTGAGCACTGGAAATACTTTTTAAAGAAAAAAAAACATGAGGGAATAAAAGAAATTCCTATCAAAAATCA
AAGTGAAATAATACCATCCAGCACTTAACTCTCAGGTCCCAACTAAGTCTGGCCTGAGCTAATTTATTTGAGCGCAGAGT
GTAAAATTTAATTCAAAATGGTGGCTATAATCACTACAGATAAATTTCATACTCTTTTGTCTTTGGAGATTCCATTGTGG
ACAGTAATACGCAGTTACAGGGTGTAGTCTGTTTAGATTCCGTAGTTCGTGGGTATCAGTTTCGGTAGAGGTGCAGCATC
GTGACACTTTTGCTAACAGGTACCACTTCTGATCACCCTGTACATACATGAGCCGAAAGGCACAATCACTGTTTCAGATT
TAAAATTATTAGTGTGTTTGTTTGGTCCAGAAACTGAGACAATCACATGACAGTCACCACGAGGAGAGAAAATTTAAAAA
ATAAAAATAAAAACAAAAAAAATTTTAAAAATTAAAAAAACAAAAATAAAGTCTAATAAGAACTTTGGTACAGGAACTTT
TTTGTAATATACATGTATGAATTGTTCATCGAGTTTTTATATTAATTTTAATTTGCTGCTAAGCAAAGACTAGGGACAGG
CAAAGATAATTTATGGCAAAGTGTTTAAATTGTTTATACATAAATAAAGTCTCTAAAACTCCTGTG

The FCTR3b polypeptide (SEQ ID NO:8) encoded by SEQ ID NO:7 is 2733 amino acid residues and is presented using the one-letter code in Table 3D. The protein has a predicted molecular weight of 303424.3 daltons.

Table 3D. Encoded FCTR3b protein sequence (SEQ ID NO:8).

MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNRVTDLIHRESDEFPRQGTNFTLAELGI
CEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTEGGMSPEHAIRLWGRGIKSRRSSGLSSRENSALTLTDSDNENKSDDENGRPIP
PTSSPSLLPSAQLPSSHNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTLRPPLPPPHNH
TLSHHHSSANSLNRNSLTNRRSQIHAPAPAPNDLATTPESVQLQDSWVLNSNVPLETRHFLFKTSSGSTPLFSSSSPGYPLTSGTV
YTPPPRLLPRNTFSRKAFKLKKPSKYCSWKCAALSAIAAALLLAILLAYFIVPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQI
HISQPQFLKFNISLGKDALFGVYIRRGLPPSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVFVQYLDVGLWHLAFYNDG
KDKEMVSFNTVVLDSVQDCPRNCHGNGECVSGVCHCFPGFLGADCAKAACPVLCSGNGQYSKGTCQCYSGWKGAECDVPMNQCIDP
SCGGHGSCIDGNCVCSAGYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDTGLCSCDPNW
MGPDCSVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTCKDGKCECREGWNGEHCTIGRQTAGTETDGCPDLCN
GNGRCTLGQNSWQCVCQTGWRGPGCNVAMETSCADNKDNEGDGLVDCLDPDCCLQSACQNSLLCRGSRDPLDIIQQGQTDWPAVKS
FYDRIKLLAGKDSTHIIPGENPFNSSLVSLIRGQVVTTDGTPLVGVNVSFVKYPKYGYTITRQDGTFDLIANGGASLTLHFERAPF
MSQERTVWLPWNSFYAMDTLVMKTEENSIPSCDLSGFVRPDPIIISSPLSTFFSAAPGQNPIVPETQVLHEEIELPGSNVKLRYLS
SRTAGYKSLLKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLSDAVVSVGFEYETCPSLILW
EKRTALLQGFELDPSNLGGWSLDKHHILNVKSGILHKGTGENQFLTQQPAIITSIMGNGRRRSISCPSCNGLAEGNKLLAPVALAV
GIDGSLYVGDFNYIRRIFPSRNVTSILELRNKEFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAG
TGEQCLPFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWP
TDLAVNPMDNSLYVLENNVILRITENHQVSIIAGRPMHCQVPGIDYSLSKLAIHSALESASAIAISHTGVLYITETDEKKINRLRQ
VTTNGEICLLAGAASDCDCKNDVNCNCYSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVLNAFNQYEAASPG
EQELYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELIDNNGNSLKIRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNL
ELGLMTYDGNTGLLATKSDETGWTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNRDDDVTVITNLSSVEASYTVVQ
DQVRNSYQLCNNGTLRVMYANGMGISFHSEPHVLAGTITPTIGRCNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLL
SIDYDRNIRTEKIYDDHRKFTLRIIYDQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGRIVSRMFADGKVWS
YSYLDKSMVLLLQSQRQYIFEYDSSDRLLAVTMPSVARHSMSTHTSIGYIRNIYNPPESNASVIFDYSDDGRILKTSFLGTGRQVF
YKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMVNLQSGGFSCTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKP
VISETPLPVDLYRYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTVQYDSMGRVIKRELK
LGPYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDLNGNLHLLNPGNSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDI
FEYNSKGLLTRAYNKASGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGHLFAMESSSGE
EYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHGGLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVG
KEPAPFNLYMFKSNNPLSSELDLKNYVTDVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQ
AFMALEGQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGRVTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYF
VKIGSADGDLVTLGTTIGRKVLESGVNVTVSQPTLLVNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQARQRALGTA
WAKEQQKARDGREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNEMGKR

In further alternative embodiments the italicized bases in the 5' end of the FCTR3b sequence in table 3C is a variable region. This region can be substituted for in other embodiments of FCTR3. The nucleotide sequence for 9823bp FCTR3c (also referred to herein as 10129612.0.154) has the same nucleotide sequence as FCTR3b except that the italicized region is replaced with the 201 base sequence shown in Table 3E. An ORF for the total FCTR3c nucleotide sequence was identified beginning with an ATG initiation codon at nucleotides 277-280 and ending with a TAG codon at nucleotides 8473-8475. This is the same open reading frame that is shown in Table 3C, with the corresponding base numbers for FCTR3c. This open reading frame will translate the same amino acid sequence as shown in Table 3C for FCTR3b.

Table 3E. Encoded FCTR3c 5'end nucleotide sequence (SEQ ID NO:9).

GCTCCAAAGCGAGCTGGGACCGAAGACTCTAGGCTAAGTTATCTATGTAGATGGTGTCAGGGAGCGAAGCTACTGACCGA
GCTGCTGTTACATCCAGCTTTTTAATTGCCTAAGCGGTCTGGGGCTTGCTTCGTCATTTGGCTTTGCTGTGGAGCACTCC
TGTAAAGCCAGCTGAATTGTACATCGAAGATCCACCCTTTT

In yet another embodiment, the italicized region shown in the 5' end of the sequence in Table 3C can be replaced with the sequence shown in Table 3F to form 9823bp FCTR3d (also referred to herein as 10129612.0.67). An ORF was identified beginning with an ATG initiation codon at nucleotides 277-280 and ending with a TAG codon at nucleotides 8473-8475. This is the same open reading frame that is shown in Table 3C, with the corresponding base numbers for FCTR3d. This open reading frame will translate the same amino acid sequence as shown in Table 3D for FCTR3b.

Table 3F. Encoded FCTR3d 5'end nucleotide sequence (SEQ ID NO:10).

GCTCCAAAGCGAGCTGGGACCGAAGACTCTAGGCTAAGTTATCTATGTAGATGGTGTCAGGGAGCGAAGCTACTGACCGA
GCTGCTGTTACATCCAGCTTTTTAATTGCCTAAGCGGTCTGGGGCTTGCTTCGTCATTTGGCTTTGCTGTGGAGCACTCC
TGTAAAGCCAGCTGAATTGTACATCGAAGATCCACCCTTTT

In yet another embodiment, the italicized region shown in the 5' end of the sequence in Table 3C can be replaced with the sequence shown in Table 3G to form 9765 bp FCTR3e (also referred to as 10129612.0.258). An ORF was identified beginning with an ATG initiation codon at nucleotides 210-212 and ending with a TAG codon at nucleotides 8408-8410. This is the same open reading frame that is shown in Table 3C, with the corresponding base numbers for FCTR3e. This open reading frame will translate the same amino acid sequence as shown in Table 3D for FCTR3b.

Table 3G. Encoded FCTR3e 5'end nucleotide sequence (SEQ ID NO:11).

CCAGCATTAGATGAGTTGACAAAAATGCAGTTTCAGCTCTGAAGGTCTGAAAGATTCTGCTGCAACTAAAGCTCTGAAGA
TTCTGCTACAACTATGACATCCATTTTCTCCCACTTCAGACAGGATGAATACAA

In yet another embodiment another FCTR3a homolog, FCTR3f (also referred to as 10129612.0.352) was found having the 9729bp sequence shown in Table 3H. An ORF was identified beginning with an ATG initiation codon at nucleotides 210-212 and ending with a TAG codon at nucleotides 8382-8384. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 3G, and the start and stop codons are in bold letters.

Table 3H. Encoded FCTR3f nucleotide sequence (SEQ ID NO:12).

CCAGCATTAGATGAGTTGACAAAAATGCAGTTTCAGCTCTGAAGGTCTGAAAGATTCTGCTGCAACTAAAGCTCTGAAGA
TTCTGCTACAACTATGACATCCATTTTCTCCCACTTCAGACAGGATGAATACAAGGTGGCAAAGTGACAAGTGCCAAAAC
TCAGGCCTGACTTTCCTGAAAACATCAGCATTCTGCCATATCTGGAATA**ATG**GATGTAAAGGACCGGCGACACCGCTCTT
TGACCAGAGGACGCTGTGGCAAAGAGTGTCGCTACACAAGCTCCTCTCTGGACAGTGAGGACTGCCGGGTGCCCACACAG
AAATCCTACAGCTCCAGTGAGACTCTGAAGGCCTATGACCATGACAGCAGGATGCACTATGGAAACCGAGTCACAGACCT
CATCCACCGGGAGTCAGATGAGTTTCCTAGACAAGGAACCAACTTCACCCTTGCCGAACTGGGCATCTGTGAGCCCTCCC
CACACCGAAGCGGCTACTGCTCCGACATGGGGATCCTTCACCAGGGCTACTCCCTTAGCACAGGGTCTGACGCCGACTCC
GACACCGAGGGAGGGATGTCTCCAGAACACGCCATCAGACTGTGGGGCAGAGGGATAAAATCCAGGCGCAGTTCCGGCCT
GTCCAGTCGTGAAAACTCGGCCCTTACCCTGACTGACTCTGACAACGAAAACAAATCAGATGATGAGAACGGTCGTCCCA
TTCCACCTACATCCTCGCCTAGTCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATAATCCTCCACCAGTTAGCTGCCAG
ATGCCATTGCTAGACAGCAACACCTCCCATCAAATCATGGACACCAACCCTGATGAGGAATTCTCCCCCAATTCATACCT
GCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCGAACCACCACAGCCAGTCGACTCTGAGGCCCC
CTCTCCCACCCCCTCACAACCACACGCTGTCCCATCACCACTCGTCCGCCAACTCCCTCAACAGGAACTCACTGACCAAT
CGGCGGAGTCAGATCCACGCCCCGGCCCCAGCGCCCAATGACCTGGCCACCACACCAGAGTCCGTTCAGCTTCAGGACAG
CTGGGTGCTAAACAGCAACGTGCCACTGGAGACCCGGCACTTCCTCTTCAAGACCTCCTCGGGGAGCACACCCTTGTTCA
GCAGCTCTTCCCCGGGATACCCTTTGACCTCAGGAACGGTTTACACGCCCCCGCCCCGCCTGCTGCCCAGGAATACTTTC
TCCAGGAAGGCTTTCAAGCTGAAGAAGCCCTCCAAATACTGCAGCTGGAAATGTGCTGCCCTCTCCGCCATTGCCGCGGC
CCTCCTCTTGGCTATTTTGCTGGCGTATTTCATAGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAG
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CCTCACTGCCGTCCGGCCGCTGAGCTGTGATTCCAGCATGGATGTAGCCCAGGTTCGTCTGGAGTGGCCAACAGACCTTG
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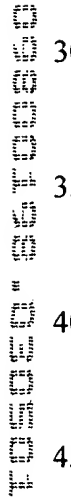

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TACGCCAGGTAACAACCAACG[redacted]GATCTGCCTTTTAGCTGGGGCAGCCTCGGACTG[redacted]CTGCAAAAACGATGTCAAT
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The FCTR3f polypeptide (SEQ ID NO:13) encoded by SEQ ID NO:12 is 2724 amino acid residues long and is presented using the one-letter code in Table 3I. This sequence differs from FCTR3b in that it is missing amino acids 758-766 from that polypeptide.

Table 3I. Encoded FCTR3f protein sequence (SEQ ID NO:13)

```
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MGPDCSVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTCKDGKCECREGWNGEHCTIDGCPDLCNGNGRCTLGQ
NSWQCVCQTGWRGPGCNVAMETSCADNKDNEGDGLVDCLDPDCCLQSACQNSLLCRGSRDPLDIIQQGQTDWPAVKSFYDRIKLLA
GKDSTHIIPGENPFNSSLVSLIRGQVVTTDGTPLVGVNVSFVKYPKYGYTITRQDGTFDLIANGGASLTLHFERAPFMSQERTVWL
PWNSFYAMDTLVMKTEENSIPSCDLSGFVRPDPIIISSPLSTFFSAAPGQNPIVPETQVLHEEIELPGSNVKLRYLSSRTAGYKSL
LKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLSDAVVSVGFEYETCPSLILWEKRTALLQG
FELDPSNLGGWSLDKHHILNVKSGILHKGTGENQFLTQQPAIITSIMGNGRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVG
DFNYIRRIFPSRNVTSILELRNKEFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGEQCLPFD
EARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMD
NSLYVLENNVILRITENHQVSIIAGRPMHCQVPGIDYSLSKLAIHSALESASAIAISHTGVLYITETDEKKINRLRQVTTNGEICL
LAGAASDCDCKNDVNCNCYSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVLNAFNQYEAASPGEQELYVFNA
DGIHQYTVSLVTGEYLYNFTYSTDNDVTELIDNNGNSLKIRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNLELGLMTYDG
NTGLLATKSDETGWTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNRDDDVTVITNLSSVEASYTVVQDQVRNSYQL
CNNGTLRVMYANGMGISFHSEPHVLAGTITPTIGRCNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIR
TEKIYDDHRKFTLRIIYDQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGRIVSRMFADGKVWSYSYLDKSMV
LLLQSQRQYIFEYDSSDRLLAVTMPSVARHSMSTHTSIGYIRNIYNPPESNASVIFDYSDDGRILKTSFLGTGRQVFYKYGKLSKL
SEIVYDSTAVTFGYDETTGVLKMVNLQSGGFSCTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLPV
DLYRYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGPYANTTK
YTYDYDGDGQLQSVAVNDRPTWRYSYDLNGNLHLLNPGNSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEYNSKGLL
TRAYNKASGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGHLFAMESSSGEEYYVASDNT
GTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHGGLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEPAPFNLY
MFKSNNPLSSELDLKNYVTDVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQAFMALEGQV
ITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGRVTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYFVKIGSADGD
LVTLGTTIGRKVLESGVNVTVSQPTLLVNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQARQRALGTAWAKEQQKAR
DGREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNEMGKR
```

In a BLASTN search it was found that the FCTR3a nucleic acid has homology to three fragments of *Mus musculus* odd Oz/ten-m homolog 2. It has 634 of 685 bases (92%) identical to bases 614-1298, 365 of 406 bases (89%) identical to bases 1420-1825, and 93 of 103 bases (90%) identical to bases 1823-1925 of *Mus musculus* odd Oz/ten-m homolog 2 (GenBank Acc: NM_011856.2) (Table 3J).

Table 3J. BLASTN of FCTR3a against *Mus musculus* odd Oz/ten-m homolog 2 (SEQ ID NO:62)

```
>GI|7657414|REF|NM_011856.2| MUS MUSCULUS ODD OZ/TEN-M HOMOLOG 2 (DROSOPHILA) (ODZ2),
MRNA
          LENGTH = 8797

 SCORE =  954 BITS (481), EXPECT = 0.0
 IDENTITIES = 634/685 (92%)
 STRAND = PLUS / PLUS

QUERY: 114  GGTCGTCCCATTCCACCTACATCCTCGCCTAGTCTCCTCCCATCTGCTCAGCTGCCTAGC 173
            ||||||||||||||||||||||||||| |||| ||||||||||||||||||||||||||
SBJCT: 614  GGTCGTCCCATTCCACCTACATCCTCGTCTAGCCTCCTCCCATCTGCTCAGCTGCCTAGC 673
```

```
QUERY: 174  TCCCATAATCCTCCACCAGTTAGCTGCCAGATGCCATTGCTAGACAGCAACACCTCCCAT 233
            ||||||||||[redacted]||||||||||||||||||||||||||||||||||[redacted]||||||||||
SBJCT: 674  TCCCATAAT[redacted]CACCAGTTAGCTGCCAGATGCCATTGCTAGACA[redacted]ACACCTCCCAT 733

QUERY: 234  CAAATCATGGACACCAACCCTGATGAGGAATTCTCCCCCAATTCATACCTGCTCAGAGCA 293
            || ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 734  CAGATCATGGACACCAACCCTGATGAGGAATTCTCCCCCAATTCATACCTGCTCAGAGCA 793

QUERY: 294  TGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCGAACCACCACAGCCAGTCGACT 353
            |||||||||||||||||||||||||||||||||||| ||||||||||||||||| ||
SBJCT: 794  TGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCAAACCACCACAGCCAGTCAACA 853

QUERY: 354  CTGAGGCCCCCTCTCCCACCCCCTCACAACCACACGCTGTCCCATCACCACTCGTCCGCC 413
            |||||||||||||| |||||||||| |||||||| |||||||| |||||||| || |||
SBJCT: 854  CTGAGGCCCCCTCTGCCACCCCCTCATAACCACACCCTGTCCCACCACCACTCCTCGGCC 913

QUERY: 414  AACTCCCTCAACAGGAACTCACTGACCAATCGGCGGAGTCAGATCCACGCCCCGGCCCCA 473
            |||||||||||||||||||||||||||||||||||| |||||||||| || ||
SBJCT: 914  AACTCCCTCAACAGGAACTCACTGACCAATCGGCGGAGTCAAATCCACGCCCCAGCTCCT 973

QUERY: 474  GCGCCCAATGACCTGGCCACCACACCAGAGTCCGTTCAGCTTCAGGACAGCTGGGTGCTA 533
            |||||||| |||||||||||||| |||||||| |||||||| ||||| ||||||||||
SBJCT: 974  GCGCCCAACGACCTGGCCACCACCCCAGAGTCTGTTCAGCTCCAGGATAGCTGGGTGCTG 1033

QUERY: 534  AACAGCAACGTGCCACTGGAGACCCGGCACTTCCTCTTCAAGACCTCCTCGGGGAGCACA 593
            ||||| ||||| |||||||||| |||||||||| ||||| || || || || ||||||
SBJCT: 1034 AACAGTAACGTCCCACTGGAGACTCGGCACTTCCTTTTCAAAACGTCGTCTGGAAGCACA 1093

QUERY: 594  CCCTTGTTCAGCAGCTCTTCCCCGGGATACCCTTTGACCTCAGGAACGGTTTACACGCCC 653
            ||| |||||||||||||||| |||||||||||||||||||| || ||||| || ||
SBJCT: 1094 CCCCTGTTCAGCAGCTCTTCTCCGGGATACCCTTTGACCTCAGGGACCGTTTATACACCA 1153

QUERY: 654  CCGCCCCGCCTGCTGCCCAGGAATACTTTCTCCAGGAAGGCTTTCAAGCTGAAGAAGCCC 713
            || |||||||||||||  ||||||| |||||||||||||| |||||||||||||| |||
SBJCT: 1154 CCACCCCGCCTGCTGCCACGGAATACATTCTCCAGGAAGGCCTTCAAGCTGAAGAAACCC 1213

QUERY: 714  TCCAAATACTGCAGCTGGAAATGTGCTGCCCTCTCCGCCATTGCCGCGGCCCTCCTCTTG 773
            |||||||||||||| |||||||||||||||| || ||||| ||||| ||||||||||||
SBJCT: 1214 TCCAAATACTGCAGTTGGAAATGTGCTGCCCTGTCTGCCATCGCCGCCGCCCTCCTCTTG 1273

QUERY: 774  GCTATTTTGCTGGCGTATTTCATAG 798
            || |||||||||| ||||||||||
SBJCT: 1274 GCCATTTTGCTGGCATATTTCATAG 1298

 SCORE =  480 BITS (242), EXPECT = E-132
 IDENTITIES = 365/406 (89%)
 STRAND = PLUS / PLUS

QUERY: 797  AGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCG 856
            |||||||||||| |||||||||||||||||||||||| ||||||||||||||||||||
SBJCT: 1420 AGTGCCCTGGTCATTGAAAAACAGCAGCATAGACAGTGGCGAAGCAGAAGTTGGTCGGCG 1479

QUERY: 857  GGTAACACAAGAAGTCCCACCAGGGGTGTTTTGGAGGTCACAAATTCACATCAGTCAGCC 916
            ||| ||||| |||||||||||||||||||||||||||| || ||||||||||||||||
SBJCT: 1480 GGTGACACAGGAAGTCCCACCAGGGGTGTTTTGGAGGTCCCAGATTCACATCAGTCAGCC 1539

QUERY: 917  CCAGTTCTTAAAGTTCAACATCTCCCTCGGGAAGGACGCTCTCTTTGGTGTTTACATAAG 976
            || |||||||||||||||||||||| || ||||| || ||||| ||||| || |||||
SBJCT: 1540 TCAATTCTTAAAGTTCAACATCTCCCTGGGCAAGGATGCCCTCTTCGGTGTCTATATAAG 1599

QUERY: 977  AAGAGGACTTCCACCATCTCATGCCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGA 1036
            |||||||| ||||| |||||||||||||||||||||||||| ||||| || |||||
SBJCT: 1600 GAGAGGACTACCACCGTCTCATGCCCAGTATGACTTCATGGAACGCCTGGATGGAAAGGA 1659

QUERY: 1037 GAAGTGGAGTGTGGTTGAGTCTCCCAGGGAACGCCGGAGCATACAGACCTTGGTTCAGAA 1096
            ||| ||||| ||||| ||||| |||||||||||||||||| |||||  |||| |||||
SBJCT: 1660 GAAATGGAGCGTGGTCGAGTCGCCCAGGGAACGCCGGAGCATCCAGACTCTGGTGCAGAA 1719

QUERY: 1097 TGAAGCCGTGTTTGTGCAGTACCTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGA 1156
            || || |||||||||||||| |||||||||||||||||| ||||||||||||||||
```

```
SBJCT: 1720 CGAGGCTGTGTTTGTGCAGTACTTGGATGTGGGCCTGTGGCACCTGGCCTTCTACAATGA 1779

QUERY: 1157 TGGAAAAGA[redacted]GAGATGGTTTCCTTCAATACTGTTGTCCTAGAT[redacted]02
                || || ||||| |||||||| |||||||| ||||||||| |||||
SBJCT: 1780 CGGCAAGGACAAGGAGATGGTCTCCTTCAACACTGTTGTCTTAGAT 1825

 SCORE =  125 BITS (63), EXPECT = 7E-26
 IDENTITIES = 93/103 (90%)
 STRAND = PLUS / PLUS

QUERY: 1258 GATTCAGTGCAGGACTGTCCACGTAACTGCCATGGGAATGGTGAATGTGTGTCCGGGGTG 1317
            ||||||||||||||||||||||| ||||| || ||||| |||||||| ||||| ||  ||
SBJCT: 1823 GATTCAGTGCAGGACTGTCCACGGAACTGTCACGGGAACGGTGAATGCGTGTCTGGACTG 1882

QUERY: 1318 TGTCACTGTTTCCCAGGATTTCTAGGAGCAGACTGTGCTAAAG 1360
            |||||||||||||||||||| ||||| ||||||||||||||||
SBJCT: 1883 TGTCACTGTTTCCCAGGATTCCTAGGTGCAGACTGTGCTAAAG 1925
```

In another BLASTN search it was found that the FCTR3a nucleic acid has homology to three fragments of *Gallus gallus* mRNA for teneurin-2. It has 541 of 629 bases (86%) identical to bases 502-1130, 302 of 367 bases (82%) identical to bases 1330-1696, and 87 of 103 bases (84%) identical to bases 1711-1813 of *Gallus gallus* mRNA for teneurin-2 (EMBL Acc: AJ245711.1) (Table 3K).

Table 3K. BLASTN of FCTR3a against *Gallus gallus* mRNA for teneurin-2 (SEQ ID NO:63)

```
>GI|6010048|EMB|AJ245711.1|GGA245711 GALLUS GALLUS MRNA FOR TENEURIN-2, SHORT SPLICE
VARIANT (TEN2 GENE)
          LENGTH = 2496

 SCORE =  549 BITS (277), EXPECT = E-153
 IDENTITIES = 541/629 (86%)
 STRAND = PLUS / PLUS

QUERY: 114  GGTCGTCCCATTCCACCTACATCCTCGCCTAGTCTCCTCCCATCTGCTCAGCTGCCTAGC 173
            |||||||||||||||||||||||||| |||| || ||||||||||||||||||| ||
SBJCT: 502  GGTCGTCCCATTCCACCTACATCCTCGTCTAGCCTTCTCCCATCTGCTCAGCTGCCCAGT 561

QUERY: 174  TCCCATAATCCTCCACCAGTTAGCTGCCAGATGCCATTGCTAGACAGCAACACCTCCCAT 233
            || ||||||||||||||||||||||||||||||||||||||||||||||||| || ||||||
SBJCT: 562  TCTCATAATCCTCCACCAGTTAGCTGCCAGATGCCATTGCTAGACAGCAATACGTCCCAT 621

QUERY: 234  CAAATCATGGACACCAACCCTGATGAGGAATTCTCCCCCAATTCATACCTGCTCAGAGCA 293
            |||||||||||||||| ||||| ||||| ||||| || |||||||||| || ||||||
SBJCT: 622  CAAATCATGGACACCAATCCTGACGAGGAGTTCTCTCCTAATTCATACCTACTAAGAGCA 681

QUERY: 294  TGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCGAACCACCACAGCCAGTCGACT 353
            || |||||||| ||||| || |||||||||||||| | ||||| |||||||||| ||
SBJCT: 682  TGTTCAGGGCCACAGCAGGCATCCAGCAGTGGCCCTTCAAACCATCACAGCCAGTCAACG 741

QUERY: 354  CTGAGGCCCCCTCTCCCACCCCCTCACAACCACACGCTGTCCCATCACCACTCGTCCGCC 413
            |||||||| |||||||| || |||||||||||| |||||||||||| |||||||| |||
SBJCT: 742  CTGAGGCCACCTCTCCCCCCTCCTCACAACCACTCGCTGTCCCATCATCACTCGTCTGCC 801

QUERY: 414  AACTCCCTCAACAGGAACTCACTGACCAATCGGCGGAGTCAGATCCACGCCCCGGCCCCA 473
            |||||||||||||||||||| || ||||| || || |  |||||||||| || || ||
SBJCT: 802  AACTCCCTCAACAGGAACTCGCTCACCAACCGCCGCAACCAGATCCACGCGCCTGCTCCC 861

QUERY: 474  GCGCCCAATGACCTGGCCACCACACCAGAGTCCGTTCAGCTTCAGGACAGCTGGGTGCTA 533
            || |||||||||||||| ||||| || ||||| || ||||| ||||||||||||||||||
SBJCT: 862  GCTCCCAATGACCTGGCGACCACGCCTGAGTCTGTGCAGCTGCAGGACAGCTGGGTGCTC 921
```

```
QUERY: 534  AACAGCAAC[redacted]CACTGGAGACCCGGCACTTCCTCTTCAAGACC[redacted]CGGGGAGCACA 593
SBJCT: 922  AACAGCAACGTGCCGCTGGAGACCAGGCATTTCTTGTTTAAGACATCTTCTGGAACGACT 981

QUERY: 594  CCCTTGTTCAGCAGCTCTTCCCCGGGATACCCTTTGACCTCAGGAACGGTTTACACGCCC 653
SBJCT: 982  CCGCTGTTCAGTAGCTCTTCCCCTGGCTACCCACTGACCTCAGGAACAGTTTATACTCCA 1041

QUERY: 654  CCGCCCCGCCTGCTGCCCAGGAATACTTTCTCCAGGAAGGCTTTCAAGCTGAAGAAGCCC 713
SBJCT: 1042 CCTCCCAGGCTGTTACCTAGAAATACATTTTCCAGGAATGCATTCAAGCTGAAAAAGCCC 1101

QUERY: 714  TCCAAATACTGCAGCTGGAAATGTGCTGC 742
SBJCT: 1102 TCCAAGTATTGTAGCTGGAAATGTGCTGC 1130

 SCORE =  212 BITS (107), EXPECT = 4E-52
 IDENTITIES = 302/367 (82%)
 STRAND = PLUS / PLUS

QUERY: 819  AGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCGGGTAACACAAGAAGTCCCACCA 878
SBJCT: 1330 AGCAGCATAGATAGTGGAGAAACAGAAGTTGGCCGCAAGGTCACCCAAGAGGTGCCCCCT 1389

QUERY: 879  GGGGTGTTTTGGAGGTCACAAATTCACATCAGTCAGCCCCAGTTCTTAAAGTTCAACATC 938
SBJCT: 1390 GGAGTGTTCTGGCGGTCTCAGATCCATATCAGCCAGCCACAGTTCCTGAAGTTCAACATA 1449

QUERY: 939  TCCCTCGGGAAGGACGCTCTCTTTGGTGTTTACATAAGAAGAGGACTTCCACCATCTCAT 998
SBJCT: 1450 TCCCTAGGGAAGGATGCTCTTTTCGGTGTTTATATAAGAAGAGGACTCCCACCATCACAT 1509

QUERY: 999  GCCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGAGAAGTGGAGTGTGGTTGAGTCT 1058
SBJCT: 1510 GCACAGTATGATTTCATGGAACGCTTGGATGGGAAAGAGAAATGGAGTGTGGTGGAATCC 1569

QUERY: 1059 CCCAGGGAACGCCGGAGCATACAGACCTTGGTTCAGAATGAAGCCGTGTTTGTGCAGTAC 1118
SBJCT: 1570 CCACGGGAACGGCGAAGTATTCAGACTCTTGTTCAGAATGAGGCTGTGTTTGTTCAGTAC 1629

QUERY: 1119 CTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGATGGAAAAGACAAAGAGATGGTT 1178
SBJCT: 1630 TTGGATGTGGGTTTGTGGCACCTGGCGTTTTACAATGATGGCAAGGACAAAGAAGTGGTC 1689

QUERY: 1179 TCCTTCA 1185
SBJCT: 1690 TCCTTCA 1696

 SCORE = 77.8 BITS (39), EXPECT = 1E-11
 IDENTITIES = 87/103 (84%)
 STRAND = PLUS / PLUS

QUERY: 1258 GATTCAGTGCAGGACTGTCCACGTAACTGCCATGGGAATGGTGAATGTGTGTCCGGGGTG 1317
SBJCT: 1711 GATTCAGTGCAAGACTGTCCACGTAATTGTCATGGCAATGGCGAGTGTGTTTCTGGTGTC 1770

QUERY: 1318 TGTCACTGTTTCCCAGGATTTCTAGGAGCAGACTGTGCTAAAG 1360
SBJCT: 1771 TGCCACTGTTTTCCCGGATTTCATGGAGCAGATTGTGCTAAAG 1813
```

In this search it was also found that the fragments of FCTR3bcd and e nucleic acids had homology to three fragments of *Homo sapiens* mRNA for KIAA1127 protein. It has 5537 of 5538 bases (99%) identical to bases 1-5538, 705 of 714 bases (98%) identical to bases 5609-

6322, and 176 of 176 bases (100%) identical to bases 6385-6560 of *Homo sapiens* mRNA for KIAA1127 protein (GenBank Acc: AB032953) (Table 3L).

Table 3L. BLASTN of FCTR3b, c, d, and e against *Homo sapiens* KIAA1127 mRNA (SEQ ID NO:64)

```
>GI|6329762|DBJ|AB032953.1|AB032953 HOMO SAPIENS MRNA FOR KIAA1127 PROTEIN, PARTIAL
CDS
          LENGTH = 6560

 SCORE = 1.097E+04 BITS (5534), EXPECT = 0.0
 IDENTITIES = 5537/5538 (99%)
 STRAND = PLUS / PLUS

QUERY: 3267 CACCTTCTTTAGTGCTGCCCCTGGGCAGAATCCCATCGTGCCTGAGACCCAGGTTCTTCA 3326
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1    CACCTTCTTTAGTGCTGCCCCTGGGCAGAATCCCATCGTGCCTGAGACCCAGGTTCTTCA 60

QUERY: 3327 TGAAGAAATCGAGCTCCCTGGTTCCAATGTGAAACTTCGCTATCTGAGCTCTAGAACTGC 3386
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 61   TGAAGAAATCGAGCTCCCTGGTTCCAATGTGAAACTTCGCTATCTGAGCTCTAGAACTGC 120

QUERY: 3387 AGGGTACAAGTCACTGCTGAAGATCACCATGACCCAGTCCACAGTGCCCCTGAACCTCAT 3446
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 121  AGGGTACAAGTCACTGCTGAAGATCACCATGACCCAGTCCACAGTGCCCCTGAACCTCAT 180

QUERY: 3447 TAGGGTTCACCTGATGGTGGCTGTCGAGGGGCATCTCTTCCAGAAGTCATTCCAGGCTTC 3506
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 181  TAGGGTTCACCTGATGGTGGCTGTCGAGGGGCATCTCTTCCAGAAGTCATTCCAGGCTTC 240

QUERY: 3507 TCCCAACCTGGCCTCCACCTTCATCTGGGACAAGACAGATGCGTATGGCCAAAGGGTGTA 3566
           |||||||||||||| ||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 241  TCCCAACCTGGCCTACACCTTCATCTGGGACAAGACAGATGCGTATGGCCAAAGGGTGTA 300

QUERY: 3567 TGGACTCTCAGATGCTGTTGTGTCTGTCGGGTTTGAATATGAGACCTGTCCCAGTCTAAT 3626
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 301  TGGACTCTCAGATGCTGTTGTGTCTGTCGGGTTTGAATATGAGACCTGTCCCAGTCTAAT 360

QUERY: 3627 TCTCTGGGAGAAAAGGACAGCCCTCCTTCAGGGATTCGAGCTGGACCCCTCCAACCTCGG 3686
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 361  TCTCTGGGAGAAAAGGACAGCCCTCCTTCAGGGATTCGAGCTGGACCCCTCCAACCTCGG 420

QUERY: 3687 TGGCTGGTCCCTAGACAAACACCACATCCTCAATGTTAAAAGTGGAATCCTACACAAAGG 3746
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 421  TGGCTGGTCCCTAGACAAACACCACATCCTCAATGTTAAAAGTGGAATCCTACACAAAGG 480

QUERY: 3747 CACTGGGGAAAACCAGTTCCTGACCCAGCAGCCTGCCATCATCACCAGCATCATGGGCAA 3806
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 481  CACTGGGGAAAACCAGTTCCTGACCCAGCAGCCTGCCATCATCACCAGCATCATGGGCAA 540

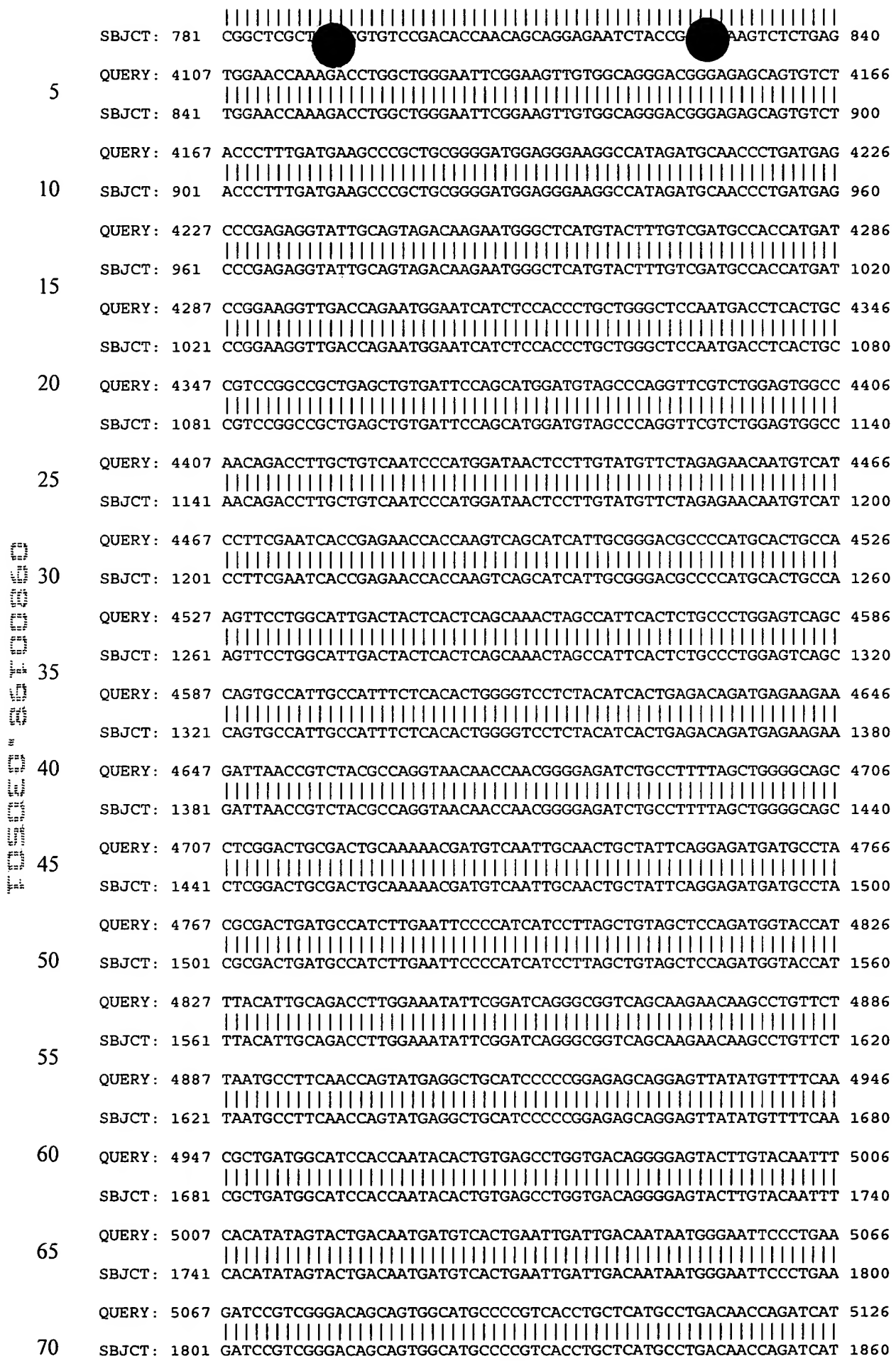
QUERY: 3807 TGGTCGCCGCCGGAGCATTTCCTGTCCCAGCTGCAACGGCCTTGCTGAAGGCAACAAGCT 3866
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 541  TGGTCGCCGCCGGAGCATTTCCTGTCCCAGCTGCAACGGCCTTGCTGAAGGCAACAAGCT 600

QUERY: 3867 GCTGGCCCCAGTGGCTCTGGCTGTTGGAATCGATGGGAGCCTCTATGTGGGTGACTTCAA 3926
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 601  GCTGGCCCCAGTGGCTCTGGCTGTTGGAATCGATGGGAGCCTCTATGTGGGTGACTTCAA 660

QUERY: 3927 TTACATCCGACGCATCTTTCCCTCTCGAAATGTGACCAGCATCTTGGAGTTACGAAATAA 3986
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 661  TTACATCCGACGCATCTTTCCCTCTCGAAATGTGACCAGCATCTTGGAGTTACGAAATAA 720

QUERY: 3987 AGAGTTTAAACATAGCAACAACCCAGCACACAAGTACTACTTGGCAGTGGACCCCGTGTC 4046
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 721  AGAGTTTAAACATAGCAACAACCCAGCACACAAGTACTACTTGGCAGTGGACCCCGTGTC 780

QUERY: 4047 CGGCTCGCTCTACGTGTCCGACACCAACAGCAGGAGAATCTACCGCGTCAAGTCTCTGAG 4106
```


SBJCT: 781 CGGCTCGCT GTGTCCGACACCAACAGCAGGAGAATCTACCG AAGTCTCTGAG 840
QUERY: 4107 TGGAACCAAAGACCTGGCTGGGAATTCGGAAGTTGTGGCAGGGACGGGAGAGCAGTGTCT 4166
SBJCT: 841 TGGAACCAAAGACCTGGCTGGGAATTCGGAAGTTGTGGCAGGGACGGGAGAGCAGTGTCT 900
QUERY: 4167 ACCCTTTGATGAAGCCCGCTGCGGGGATGGAGGGAAGGCCATAGATGCAACCCTGATGAG 4226
SBJCT: 901 ACCCTTTGATGAAGCCCGCTGCGGGGATGGAGGGAAGGCCATAGATGCAACCCTGATGAG 960
QUERY: 4227 CCCGAGAGGTATTGCAGTAGACAAGAATGGGCTCATGTACTTTGTCGATGCCACCATGAT 4286
SBJCT: 961 CCCGAGAGGTATTGCAGTAGACAAGAATGGGCTCATGTACTTTGTCGATGCCACCATGAT 1020
QUERY: 4287 CCGGAAGGTTGACCAGAATGGAATCATCTCCACCCTGCTGGGCTCCAATGACCTCACTGC 4346
SBJCT: 1021 CCGGAAGGTTGACCAGAATGGAATCATCTCCACCCTGCTGGGCTCCAATGACCTCACTGC 1080
QUERY: 4347 CGTCCGGCCGCTGAGCTGTGATTCCAGCATGGATGTAGCCCAGGTTCGTCTGGAGTGGCC 4406
SBJCT: 1081 CGTCCGGCCGCTGAGCTGTGATTCCAGCATGGATGTAGCCCAGGTTCGTCTGGAGTGGCC 1140
QUERY: 4407 AACAGACCTTGCTGTCAATCCCATGGATAACTCCTTGTATGTTCTAGAGAACAATGTCAT 4466
SBJCT: 1141 AACAGACCTTGCTGTCAATCCCATGGATAACTCCTTGTATGTTCTAGAGAACAATGTCAT 1200
QUERY: 4467 CCTTCGAATCACCGAGAACCACCAAGTCAGCATCATTGCGGGACGCCCCATGCACTGCCA 4526
SBJCT: 1201 CCTTCGAATCACCGAGAACCACCAAGTCAGCATCATTGCGGGACGCCCCATGCACTGCCA 1260
QUERY: 4527 AGTTCCTGGCATTGACTACTCACTCAGCAAACTAGCCATTCACTCTGCCCTGGAGTCAGC 4586
SBJCT: 1261 AGTTCCTGGCATTGACTACTCACTCAGCAAACTAGCCATTCACTCTGCCCTGGAGTCAGC 1320
QUERY: 4587 CAGTGCCATTGCCATTTCTCACACTGGGGTCCTCTACATCACTGAGACAGATGAGAAGAA 4646
SBJCT: 1321 CAGTGCCATTGCCATTTCTCACACTGGGGTCCTCTACATCACTGAGACAGATGAGAAGAA 1380
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SBJCT: 1501 CGCGACTGATGCCATCTTGAATTCCCCATCATCCTTAGCTGTAGCTCCAGATGGTACCAT 1560
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SBJCT: 1561 TTACATTGCAGACCTTGGAAATATTCGGATCAGGGCGGTCAGCAAGAACAAGCCTGTTCT 1620
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SBJCT: 1621 TAATGCCTTCAACCAGTATGAGGCTGCATCCCCCGGAGAGCAGGAGTTATATGTTTTCAA 1680
QUERY: 4947 CGCTGATGGCATCCACCAATACACTGTGAGCCTGGTGACAGGGGAGTACTTGTACAATTT 5006
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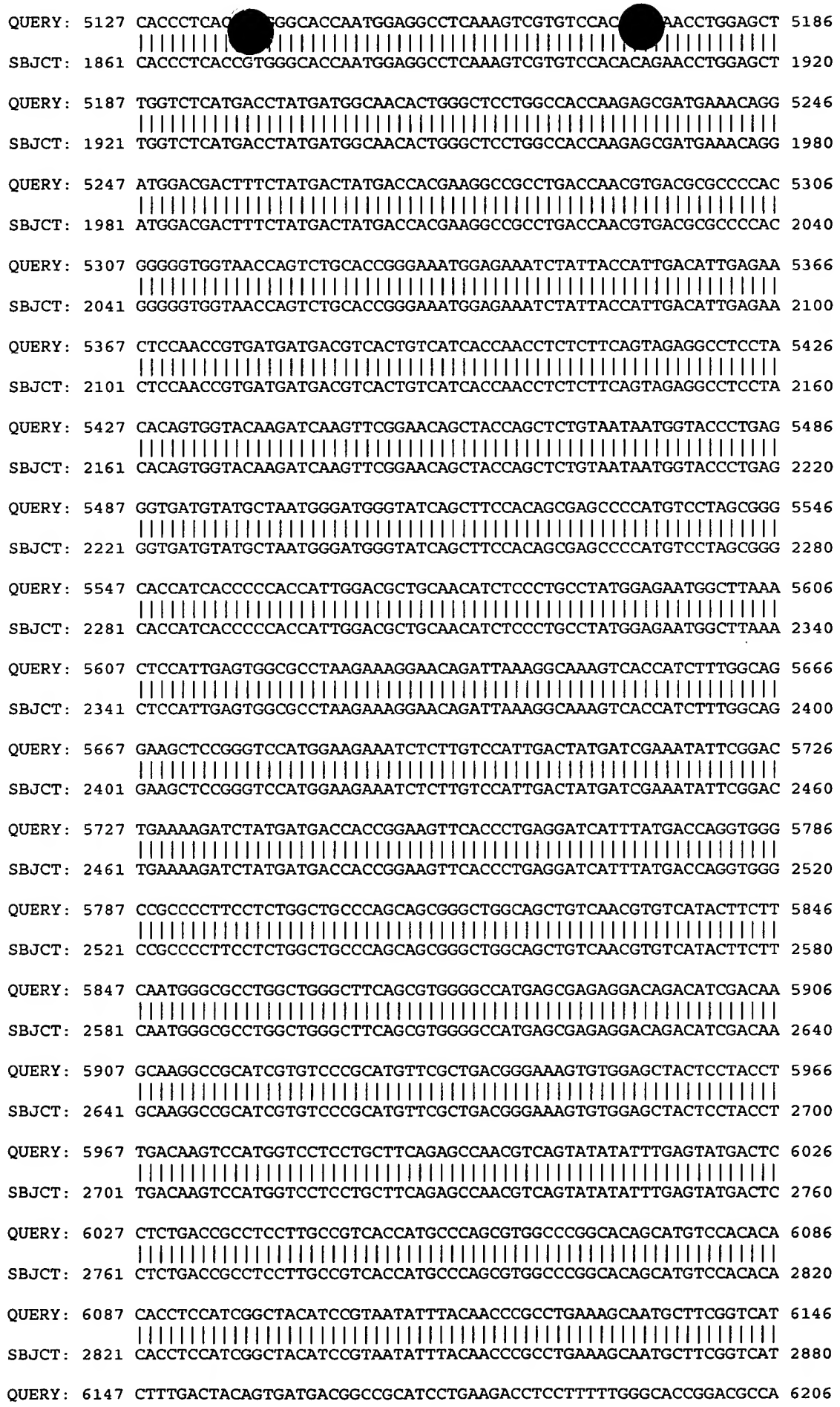
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SBJCT: 1981 ATGGACGACTTTCTATGACTATGACCACGAAGGCCGCCTGACCAACGTGACGCGCCCCAC 2040
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SBJCT: 2401 GAAGCTCCGGGTCCATGGAAGAAATCTCTTGTCCATTGACTATGATCGAAATATTCGGAC 2460
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SBJCT: 2821 CACCTCCATCGGCTACATCCGTAATATTTACAACCCGCCTGAAAGCAATGCTTCGGTCAT 2880
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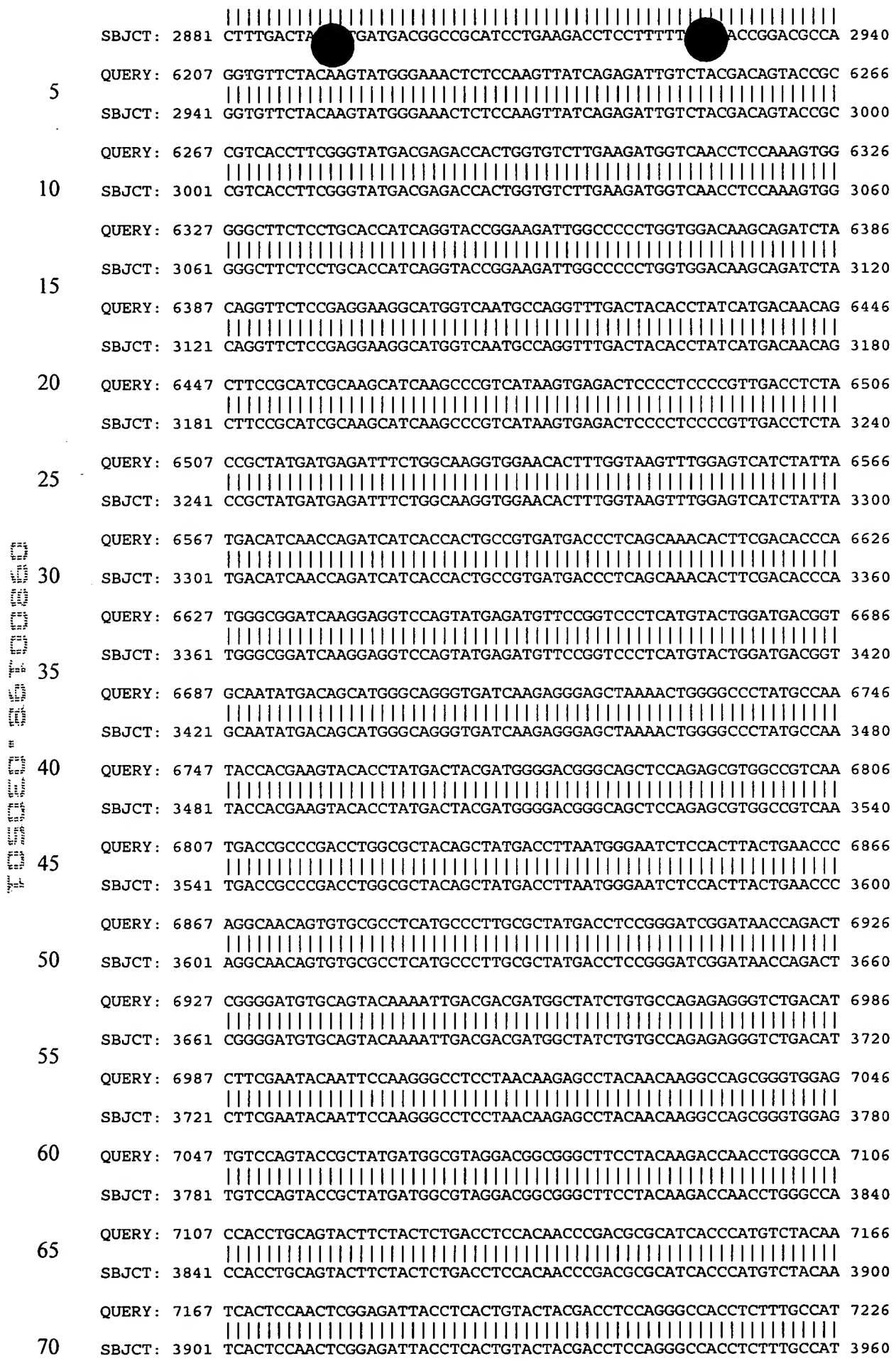
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SBJCT: 3001 CGTCACCTTCGGGTATGACGAGACCACTGGTGTCTTGAAGATGGTCAACCTCCAAAGTGG 3060
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SBJCT: 3061 GGGCTTCTCCTGCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTA 3120
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QUERY: 6507 CCGCTATGATGAGATTTCTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCATCTATTA 6566
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SBJCT: 3301 TGACATCAACCAGATCATCACCACTGCCGTGATGACCCTCAGCAAACACTTCGACACCCA 3360
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QUERY: 6867 AGGCAACAGTGTGCGCCTCATGCCCTTGCGCTATGACCTCCGGGATCGGATAACCAGACT 6926
SBJCT: 3601 AGGCAACAGTGTGCGCCTCATGCCCTTGCGCTATGACCTCCGGGATCGGATAACCAGACT 3660
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SBJCT: 3661 CGGGGATGTGCAGTACAAAATTGACGACGATGGCTATCTGTGCCAGAGAGGGTCTGACAT 3720
QUERY: 6987 CTTCGAATACAATTCCAAGGGCCTCCTAACAAGAGCCTACAACAAGGCCAGCGGGTGGAG 7046
SBJCT: 3721 CTTCGAATACAATTCCAAGGGCCTCCTAACAAGAGCCTACAACAAGGCCAGCGGGTGGAG 3780
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SBJCT: 3781 TGTCCAGTACCGCTATGATGGCGTAGGACGGCGGGCTTCCTACAAGACCAACCTGGGCCA 3840
QUERY: 7107 CCACCTGCAGTACTTCTACTCTGACCTCCACAACCCGACGCGCATCACCCATGTCTACAA 7166
SBJCT: 3841 CCACCTGCAGTACTTCTACTCTGACCTCCACAACCCGACGCGCATCACCCATGTCTACAA 3900
QUERY: 7167 TCACTCCAACTCGGAGATTACCTCACTGTACTACGACCTCCAGGGCCACCTCTTTGCCAT 7226
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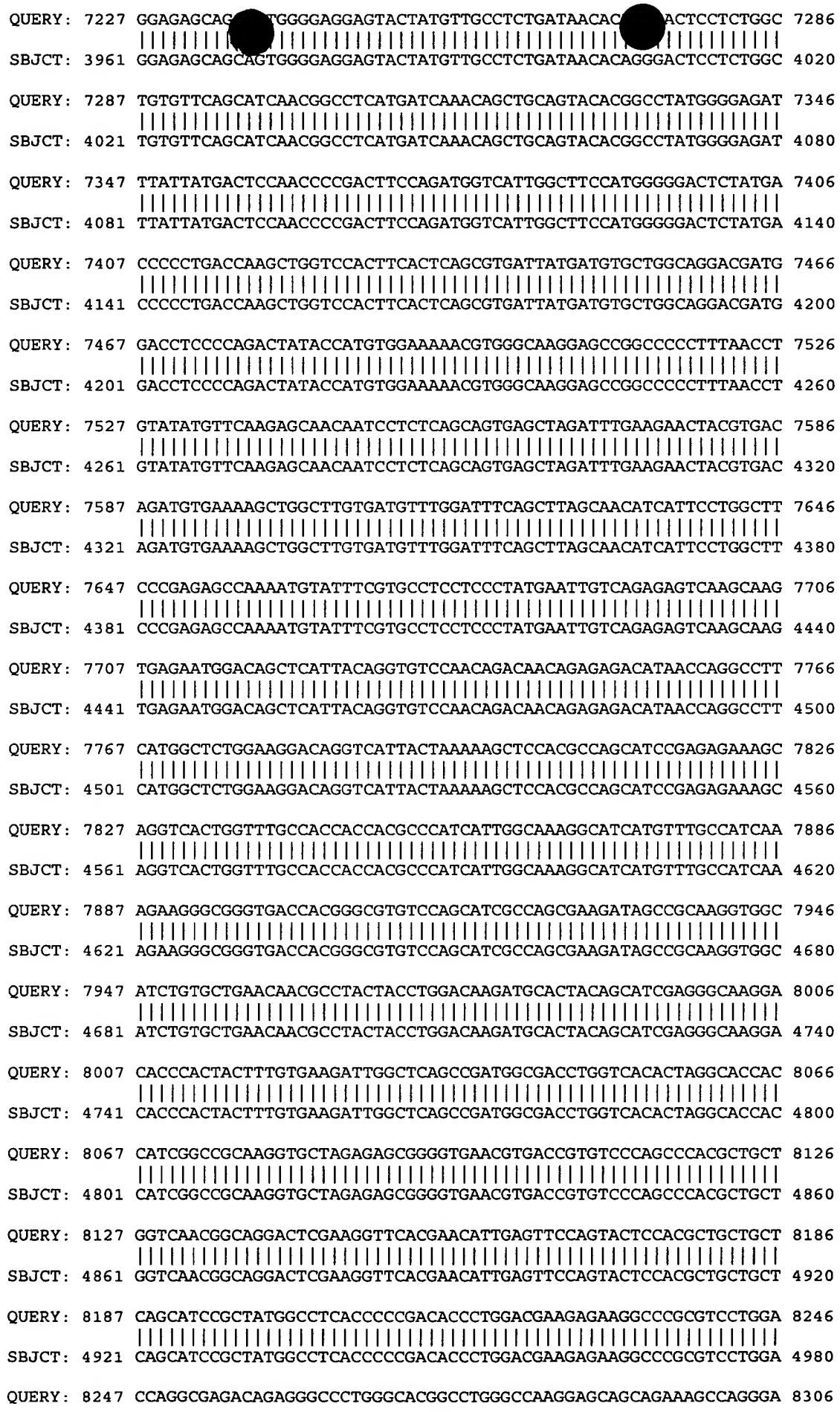
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SBJCT: 4081 TTATTATGACTCCAACCCCGACTTCCAGATGGTCATTGGCTTCCATGGGGGACTCTATGA 4140
QUERY: 7407 CCCCCTGACCAAGCTGGTCCACTTCACTCAGCGTGATTATGATGTGCTGGCAGGACGATG 7466
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QUERY: 7707 TGAGAATGGACAGCTCATTACAGGTGTCCAACAGACAACAGAGAGACATAACCAGGCCTT 7766
SBJCT: 4441 TGAGAATGGACAGCTCATTACAGGTGTCCAACAGACAACAGAGAGACATAACCAGGCCTT 4500
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SBJCT: 4501 CATGGCTCTGGAAGGACAGGTCATTACTAAAAAGCTCCACGCCAGCATCCGAGAGAAAGC 4560
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QUERY: 7887 AGAAGGGCGGGTGACCACGGGCGTGTCCAGCATCGCCAGCGAAGATAGCCGCAAGGTGGC 7946
SBJCT: 4621 AGAAGGGCGGGTGACCACGGGCGTGTCCAGCATCGCCAGCGAAGATAGCCGCAAGGTGGC 4680
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SBJCT: 4681 ATCTGTGCTGAACAACGCCTACTACCTGGACAAGATGCACTACAGCATCGAGGGCAAGGA 4740
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QUERY: 8247 CCAGGCGAGACAGAGGGCCCTGGGCACGGCCTGGGCCAAGGAGCAGCAGAAAGCCAGGGA 8306

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QUERY: 8307 CGGGAGAGAGGGGAGCCGCCTGTGGACTGAGGGCGAGAAGCAGCAGCTTCTGAGCACCGG 8366
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QUERY: 8607 AGAAAGCTCACATTTTTTGAGTTCAAATGCTACTGTCCAAGCGAGAAGTCCCTCATCCTG 8666
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QUERY: 8667 AAGTAGACTAAAGCCCGGCTGAAAATTCCGAGGAAAACAAAACAAACGAATGAATGAACA 8726
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QUERY: 8727 GACACACACAATGTTCCAAGTTCCCCTAAAATATGACCCACTTGTTCTGGGTCTACGCAG 8786
SBJCT: 5461 GACACACACAATGTTCCAAGTTCCCCTAAAATATGACCCACTTGTTCTGGGTCTACGCAG 5520

QUERY: 8787 AAAAGAGACGCAAAGTGT 8804
SBJCT: 5521 AAAAGAGACGCAAAGTGT 5538

SCORE = 1362 BITS (687), EXPECT = 0.0
 IDENTITIES = 705/714 (98%)
 STRAND = PLUS / PLUS

QUERY: 8875 CACGGACCGATAAACAAAGAAGCGAAGATAAGAAAGAAGGCCTCATATCCAATTACCTCA 8934
SBJCT: 5609 CACGGACCGATAAACAAAGAAGCGAAGATAAGAAAGAAGGCCTCATATCCAATTACCTCA 5668

QUERY: 8935 CTCATTCACATGTGAGCGACACGCAGACATCCGCGAGGGCCAGCGTCACCAGACCAGCTG 8994
SBJCT: 5669 CTCATTCACATGTGAGCGACACGCAGACATCCGCGAGGGCCAGCGTCACCAGACCAGCTG 5728

QUERY: 8995 CGGGACAAACCACTCAGACTGCTTGTAGGACAAATACTTCTGACATTTTCGTTTAAGCAA 9054
SBJCT: 5729 CGGGACAAACCACTCAGACTGCTTGTAGGACAAATACTTCTGACATTTTCGTTTAAGCAA 5788

QUERY: 9055 ATACAGGTGCATTTAAAACACGACTTTGGGGGTGATTTGTGTGTAGCGCCTGGGGAGGGG 9114
SBJCT: 5789 ATACAGGTGCATTTAAAACACGACTTTGGGGGTGATTTGTGTGTAGCGCCTGGGGAGGGG 5848

QUERY: 9115 GGATAAAAGAGGAGGAGTGAGCACTGGAAATACTTTTTAAAGNNNNNNNNNCATGAGGGA 9174
SBJCT: 5849 GGATAAAAGAGGAGGAGTGAGCACTGGAAATACTTTTTAAAGAAAAAAAAAACATGAGGGA 5908

QUERY: 9175 ATAAAAGAAATTCCTATCAAAAATCAAAGTGAAATAATACCATCCAGCACTTAACTCTCA 9234
SBJCT: 5909 ATAAAAGAAATTCCTATCAAAAATCAAAGTGAAATAATACCATCCAGCACTTAACTCTCA 5968

QUERY: 9235 GGTCCCAACTAAGTCTGGCCTGAGCTAATTTATTTGAGCGCAGAGTGTAAAATTTAATTC 9294
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QUERY: 9295 AAAATGGTG[redacted]TAATCACTACAGATAAATTTCATACTCTTTTG[redacted]TGGAGATTCCA 9354
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QUERY: 9355 TTGTGGACAGTAATACGCAGTTACAGGGTGTAGTCTGTTTAGATTCCGTAGTTCGTGGGT 9414
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QUERY: 9475 ACCCTGTACATACATGAGCCGAAAGGCACAATCACTGTTTCAGATTTAAAATTATTAGTG 9534
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QUERY: 9535 TGTTTGTTTGGTCCAGAAACTGAGACAATCACATGACAGTCACCACGAGGAGAG 9588
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 6269 TGTTTGTTTGGTCCAGAAACTGAGACAATCACATGACAGTCACCACGAGGAGAG 6322

SCORE =  349 BITS (176), EXPECT = 2E-92
 IDENTITIES = 176/176 (100%)
 STRAND = PLUS / PLUS

QUERY: 9651 GTCTAATAAGAACTTTGGTACAGGAACTTTTTTGTAATATACATGTATGAATTGTTCATC 9710
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 6385 GTCTAATAAGAACTTTGGTACAGGAACTTTTTTGTAATATACATGTATGAATTGTTCATC 6444

QUERY: 9711 GAGTTTTTATATTAATTTTAATTTGCTGCTAAGCAAAGACTAGGGACAGGCAAAGATAAT 9770
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 6445 GAGTTTTTATATTAATTTTAATTTGCTGCTAAGCAAAGACTAGGGACAGGCAAAGATAAT 6504

QUERY: 9771 TTATGGCAAAGTGTTTAAATTGTTTATACATAAATAAAGTCTCTAAAACTCCTGTG 9826
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SBJCT: 6505 TTATGGCAAAGTGTTTAAATTGTTTATACATAAATAAAGTCTCTAAAACTCCTGTG 6560
```

In this search it was also found that the FCTR3bcd and e nucleic acids had homology to five fragments of *Mus musculus* mRNA for Ten-m2. It has 5498 of 6108 bases (90%) identical to bases 2504-8610, 1095 of 1196 bases (91%) identical to bases 103-1298, 1000 of 1088 bases (91%) identical to bases 1420-2540, 81 of 89 bases (91%) identical to bases 8655-8743, and 30 of 32 bases (93%) identical to bases 7-38 of *Mus musculus* mRNA for Ten-m2 (Table 3M).

Table 3M. BLASTN of FCTR3b, c, d, and e against *Mus musculus* mRNA for Ten-m2 Mrna (SEQ ID NO:65)

```
>GI|4760777|DBJ|AB025411.1|AB025411 MUS MUSCULUS MRNA FOR TEN-M2, COMPLETE CDS
          LENGTH = 8797

 SCORE = 7263 BITS (3664), EXPECT = 0.0
 IDENTITIES = 5498/6108 (90%), GAPS = 1/6108 (0%)
 STRAND = PLUS / PLUS

QUERY: 2578 GATGGCTGCCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGTCAGAACAGCTGG 2637
           |||||||||||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 2504 GATGGCTGCCCTGATTTGTGCAACGGTAACGGGAGATGCACACTGGGTCAGAACAGCTGG 2563

QUERY: 2638 CAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCCGGATGCAACGTTGCCATGGAAACTTCC 2697
           |||||||||||||||||||||||||||||||| |||||||||||||||||||||| |||
SBJCT: 2564 CAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCTGGATGCAACGTTGCCATGGAAACCTCC 2623

QUERY: 2698 TGTGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGATTGTTTGGACCCTGACTGC 2757
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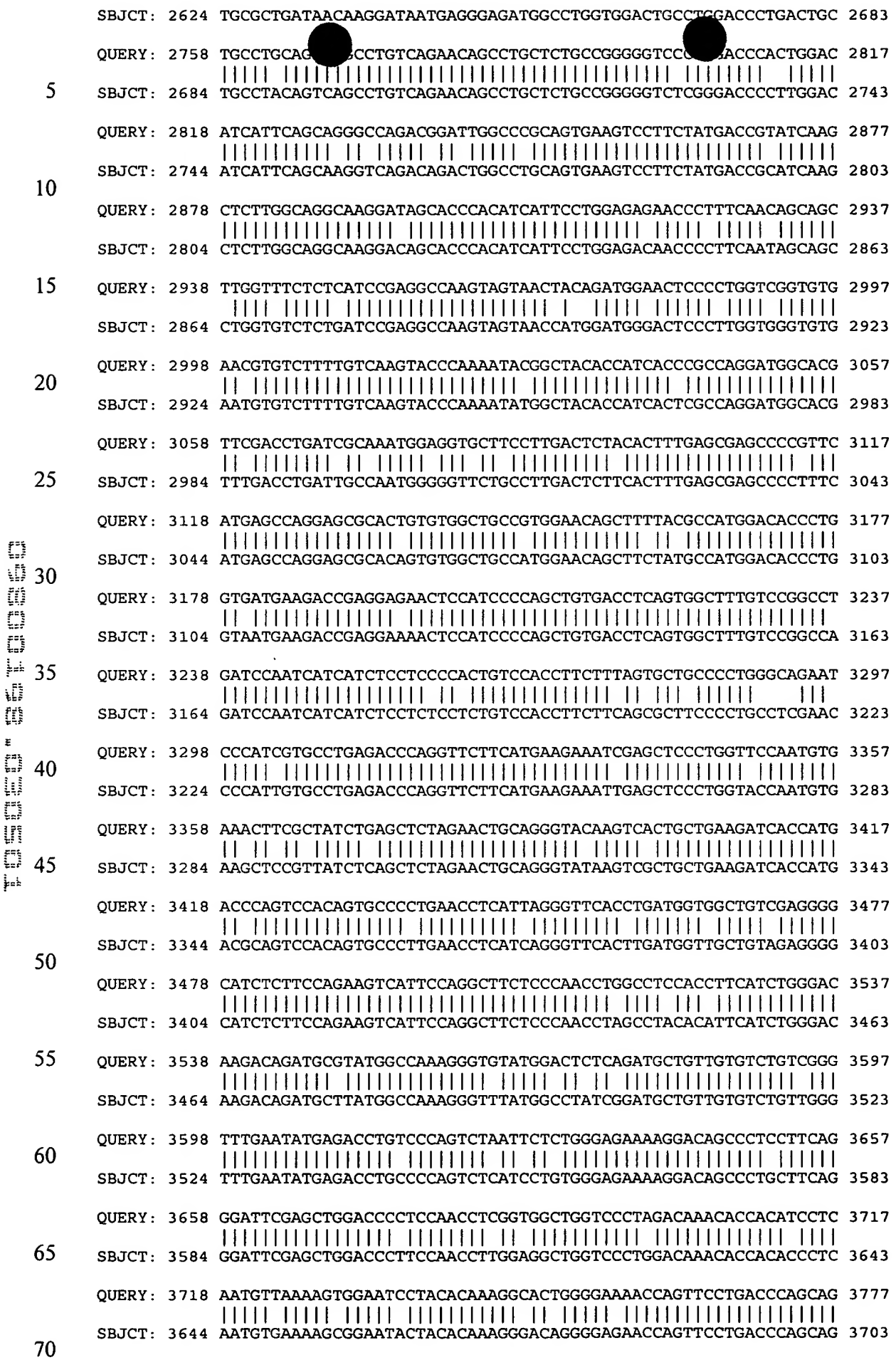
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QUERY: 2878 CTCTTGGCAGGCAAGGATAGCACCCACATCATTCCTGGAGAGAACCCTTTCAACAGCAGC 2937
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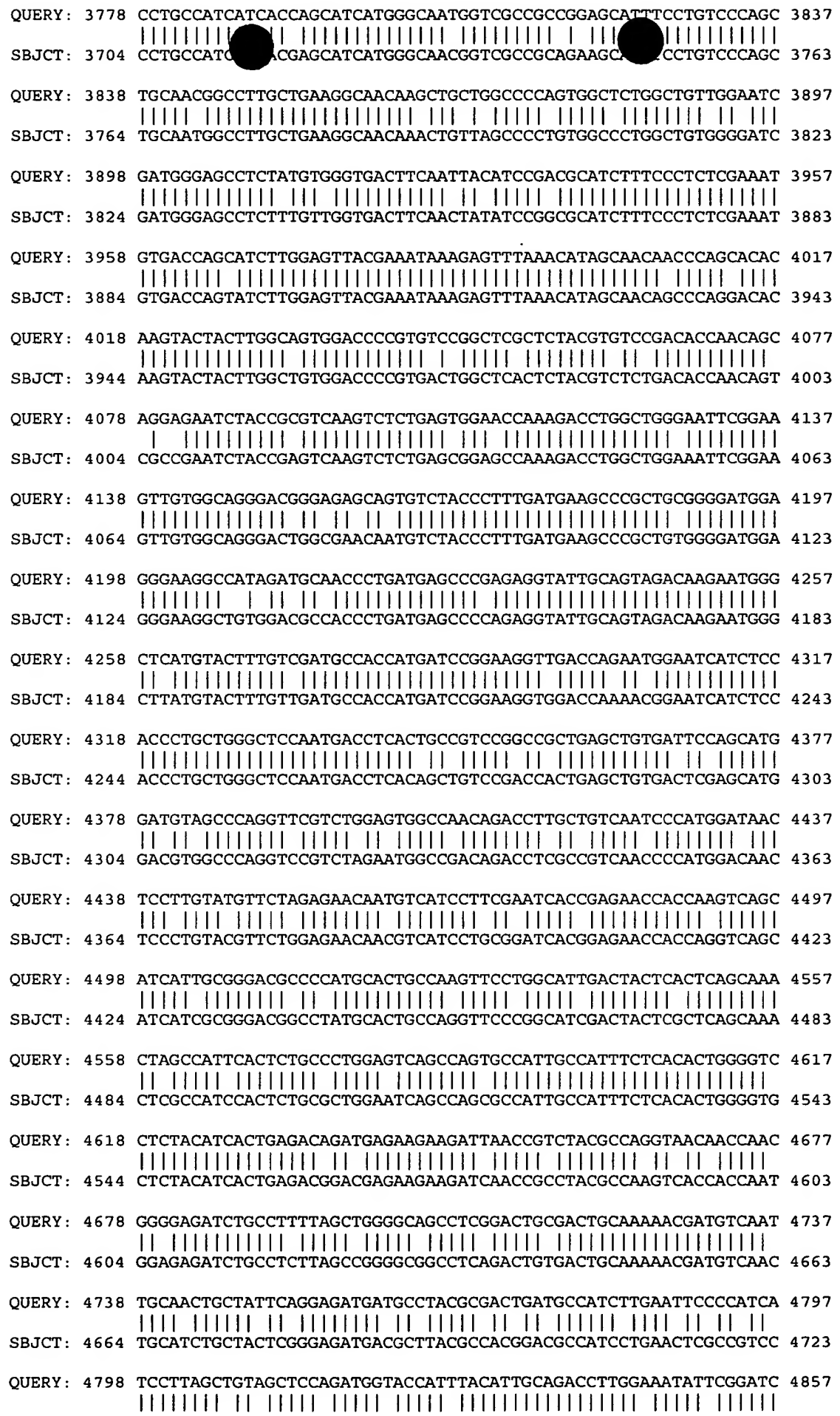
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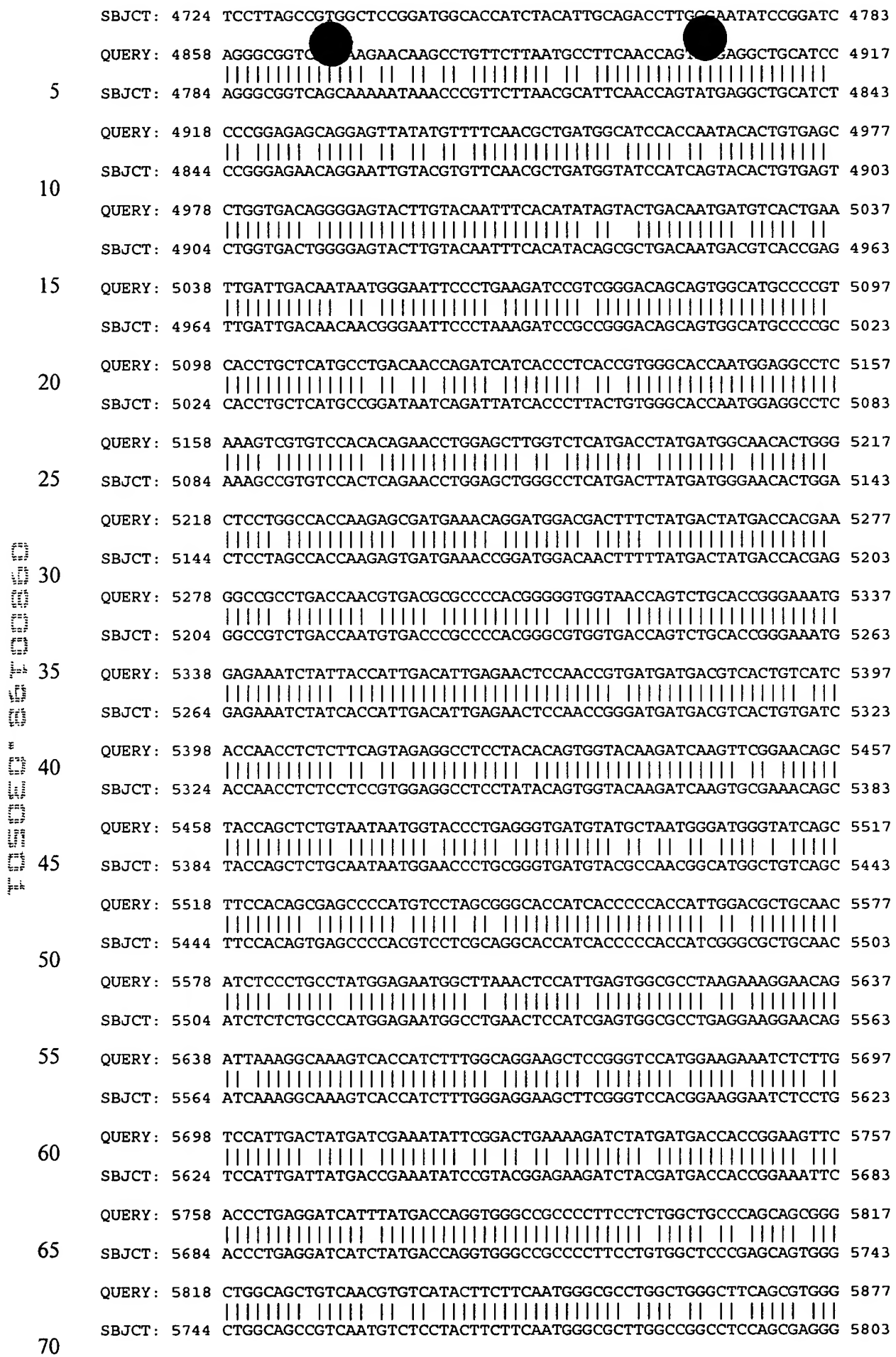
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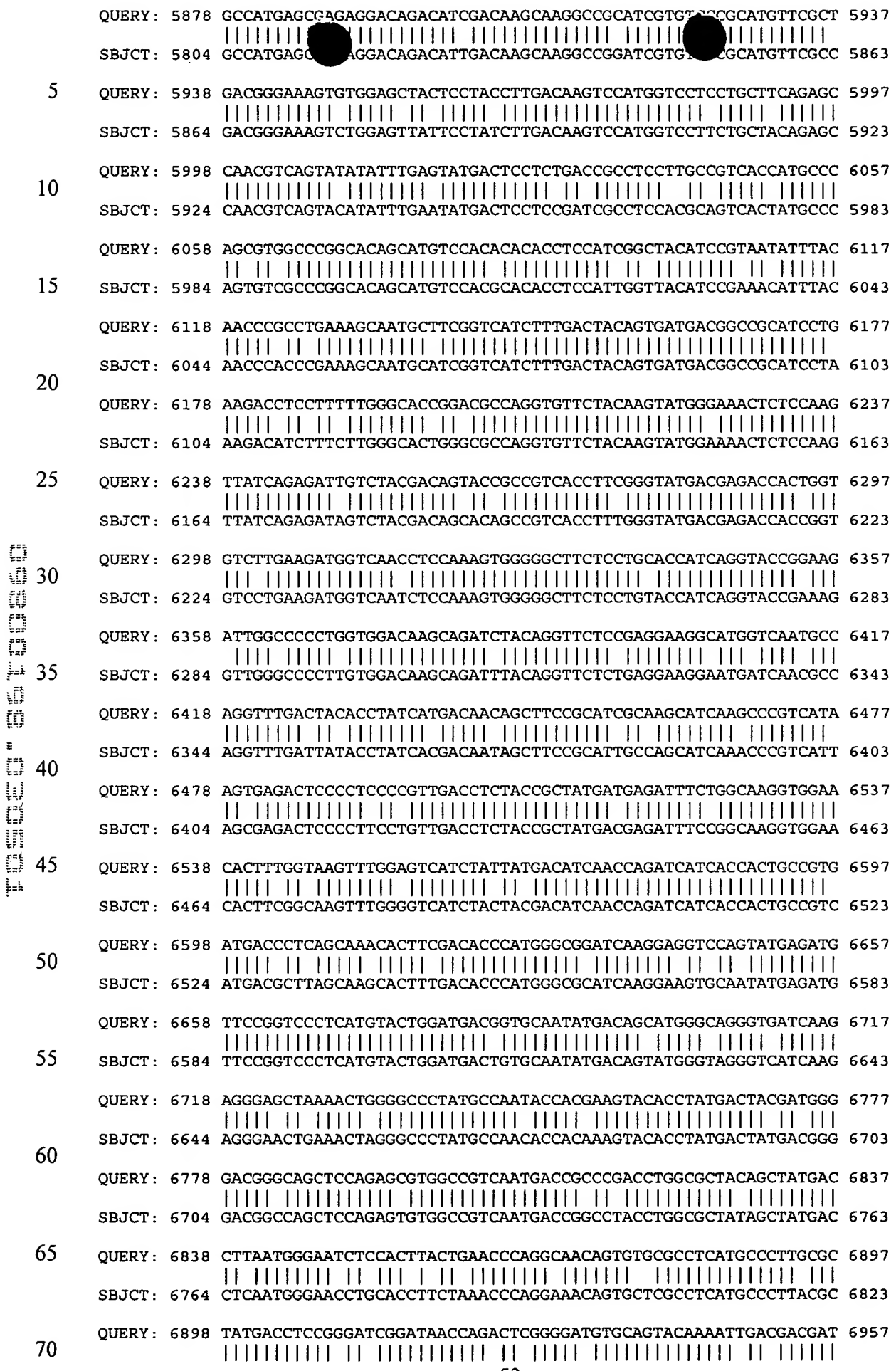
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QUERY: 8518 CAGCAGGAGTAACTGTTATCTCCTCTCCTAAGGAGATGAAGACCTAACAGGGGCACTGCG 8577
           ||||||||| |||||| | |||||||||||||||| |||||||||| ||||||||| |
SBJCT: 8444 CAGCAGGAGCAACTGTGACCTCCTCTCCTAAGGAGACGAAGACCTAAC-GGGGCACTGAG 8502

QUERY: 8578 GCTGGGCTGCTTTAGGAGACCAAGTGGCAAGAAAGCTCACATTTTTTGAGTTCAAATGCT 8637
           || ||||||||||||||  ||||||||||||||||||||||||||||||||||||||||
SBJCT: 8503 GCCGGGCTGCTTTAGGATCCCAAGTGGCAAGAAAGCTCACATTTTTTGAGTTCAAATGCT 8562

QUERY: 8638 ACTGTCCAAGCGAGAAGTCCCTCATCCTGAAGTAGACTAAAGCCCGGC 8685
           |||||| |||||  |||||||||||||||||||||||| ||||||||
SBJCT: 8563 ACTGTCTAAGCGCAAAGTCCCTCATCCTGAAGTAGACTAGAGCCCGGC 8610

 SCORE = 1570 BITS (792), EXPECT = 0.0
 IDENTITIES = 1095/1196 (91%)
 STRAND = PLUS / PLUS

QUERY: 270  ATCTGGAATAATGGATGTAAAGGACCGGCGACACCGCTCTTTGACCAGAGGACGCTGTGG 329
           |||||||||||||||||||||||||||||||| |||||||||||||| ||||| |||||
SBJCT: 103  ATCTGGAATAATGGATGTAAAGGACCGGCGACATCGCTCTTTGACCAGGGGACGGTGTGG 162

QUERY: 330  CAAAGAGTGTCGCTACACAAGCTCCTCTCTGGACAGTGAGGACTGCCGGGTGCCCACACA 389
           |||||||||||||||||| |||||||||||||||||||||||||||| |||||||| ||
SBJCT: 163  CAAAGAGTGTCGCTACACCAGCTCCTCTCTGGACAGTGAGGACTGCCGTGTGCCCACTCA 222

QUERY: 390  GAAATCCTACAGCTCCAGTGAGACTCTGAAGGCCTATGACCATGACAGCAGGATGCACTA 449
           ||| |||||||| |||||||||  ||||||| |||||||||||||||| ||||||||
SBJCT: 223  GAAGTCCTACAGTTCCAGTGAGACCTTGAAGGCTTATGACCATGACAGCAGAATGCACTA 282

QUERY: 450  TGGAAACCGAGTCACAGACCTCATCCACCGGGAGTCAGATGAGTTTCCTAGACAAGGAAC 509
           |||||||||||||||||||  | |||||||||| ||||||||| |||||||||| ||
SBJCT: 283  TGGAAACCGAGTCACAGACCTGGTGCACCGGGAGTCCGATGAGTTTTCTAGACAAGGGAC 342

QUERY: 510  CAACTTCACCCTTGCCGAACTGGGCATCTGTGAGCCCTCCCCACACCGAAGCGGCTACTG 569
           |||||||||| || ||| |||| ||||| |||||||||||||||||| || |||||
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SBJCT: 343  AAACTTCACCCTGGCAGAATTGGGAATCTGCGAGCCCTCCCCACACCGAAGTGGTTACTG 402

QUERY: 570  CTCCGACAT[redacted]ATCCTTCACCAGGGCTACTCCCTTAGCACAGG[redacted]GACGCCGACTC 629
            ||||||||||| ||||| |||||||||||||||| ||||| |||||||| || |||||
SBJCT: 403  TTCCGACATGGGTATCCTCCACCAGGGCTACTCCCTGAGCACTGGGTCTGATGCAGACTC 462

QUERY: 630  CGACACCGAGGGAGGGATGTCTCCAGAACACGCCATCAGACTGTGGGGCAGAGGGATAAA 689
            |||||||||||||||||||||||||||| |||||||||||||||| ||||||||||
SBJCT: 463  GGACACCGAGGGAGGGATGTCTCCAGAACATGCCATCAGACTGTGGGGACGAGGGATAAA 522

QUERY: 690  ATCCAGGCGCAGTTCCGGCCTGTCCAGTCGTGAAAACTCGGCCCTTACCCTGACTGACTC 749
            |||||||||||| || ||| ||||||| || || |||||||||||||| ||||||||||
SBJCT: 523  ATCCAGGCGCAGCTCTGGCTTGTCCAGCCGCGAGAACTCGGCCCTTACTCTGACTGACTC 582

QUERY: 750  TGACAACGAAAACAAATCAGATGATGAGAACGGTCGTCCCATTCCACCTACATCCTCGCC 809
            |||||| ||||| ||||| ||||| || || |||||||||||||||||||||||||| |
SBJCT: 583  TGACAATGAAAATAAATCGGATGACGACAATGGTCGTCCCATTCCACCTACATCCTCGTC 642

QUERY: 810  TAGTCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATAATCCTCCACCAGTTAGCTGCCA 869
            ||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 643  TAGCCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATAATCCTCCACCAGTTAGCTGCCA 702

QUERY: 870  GATGCCATTGCTAGACAGCAACACCTCCCATCAAATCATGGACACCAACCCTGATGAGGA 929
            |||||||||||||||||||||||||||||||| ||||||||||||||||||||||||||
SBJCT: 703  GATGCCATTGCTAGACAGCAACACCTCCCATCAGATCATGGACACCAACCCTGATGAGGA 762

QUERY: 930  ATTCTCCCCCAATTCATACCTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGCAG 989
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 763  ATTCTCCCCCAATTCATACCTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGCAG 822

QUERY: 990  TGGCCCTCCGAACCACCACAGCCAGTCGACTCTGAGGCCCCCTCTCCCACCCCCTCACAA 1049
            ||||||||| |||||||||||||||| || |||||||||||||| |||||||||| ||
SBJCT: 823  TGGCCCTCCAAACCACCACAGCCAGTCAACACTGAGGCCCCCTCTGCCACCCCCTCATAA 882

QUERY: 1050 CCACACGCTGTCCCATCACCACTCGTCCGCCAACTCCCTCAACAGGAACTCACTGACCAA 1109
            |||||| |||||||| |||||||| || ||||||||||||||||||||||||||||||
SBJCT: 883  CCACACCCTGTCCCACCACCACTCCTCGGCCAACTCCCTCAACAGGAACTCACTGACCAA 942

QUERY: 1110 TCGGCGGAGTCAGATCCACGCCCCGGCCCCAGCGCCCAATGACCTGGCCACCACACCAGA 1169
            |||||||||||| |||||||||| || || |||||||| |||||||||||||| |||||
SBJCT: 943  TCGGCGGAGTCAAATCCACGCCCCAGCTCCTGCGCCCAACGACCTGGCCACCACCCCAGA 1002

QUERY: 1170 GTCCGTTCAGCTTCAGGACAGCTGGGTGCTAAACAGCAACGTGCCACTGGAGACCCGGCA 1229
            ||| |||||||| ||||| |||||||||||| ||||| ||||| |||||||||||| |||||
SBJCT: 1003 GTCTGTTCAGCTCCAGGATAGCTGGGTGCTGAACAGTAACGTCCCACTGGAGACTCGGCA 1062

QUERY: 1230 CTTCCTCTTCAAGACCTCCTCGGGGAGCACACCCTTGTTCAGCAGCTCTTCCCCGGGATA 1289
            |||||| ||||| || || || || ||||||||| |||||||||||||||| ||||||||
SBJCT: 1063 CTTCCTTTTCAAAACGTCGTCTGGAAGCACACCCCTGTTCAGCAGCTCTTCTCCGGGATA 1122

QUERY: 1290 CCCTTTGACCTCAGGAACGGTTTACACGCCCCCGCCCCGCCTGCTGCCCAGGAATACTTT 1349
            |||||||||||||||| || ||||| || || || |||||||||||||| ||||||| ||
SBJCT: 1123 CCCTTTGACCTCAGGGACCGTTTATACACCACCACCCCGCCTGCTGCCACGGAATACATT 1182

QUERY: 1350 CTCCAGGAAGGCTTTCAAGCTGAAGAAGCCCTCCAAATACTGCAGCTGGAAATGTGCTGC 1409
            |||||||||||| |||||||||||||| |||||||||||||||| ||||||||||||||
SBJCT: 1183 CTCCAGGAAGGCCTTCAAGCTGAAGAAACCCTCCAAATACTGCAGTTGGAAATGTGCTGC 1242

QUERY: 1410 CCTCTCCGCCATTGCCGCGGCCCTCCTCTTGGCTATTTTGCTGGCGTATTTCATAG 1465
            ||| || ||||| ||||| |||||||||||||| |||||||||| ||||||||||
SBJCT: 1243 CCTGTCTGCCATCGCCGCCGCCCTCCTCTTGGCCATTTTGCTGGCATATTTCATAG 1298

 SCORE = 1455 BITS (734), EXPECT = 0.0
 IDENTITIES = 1000/1088 (91%), GAPS = 3/1088 (0%)
 STRAND = PLUS / PLUS

QUERY: 1464 AGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCG 1523
            |||||||||||| |||||||||||||||||||||||| ||||||||||||||||||||
SBJCT: 1420 AGTGCCCTGGTCATTGAAAAACAGCAGCATAGACAGTGGCGAAGCAGAAGTTGGTCGGCG 1479
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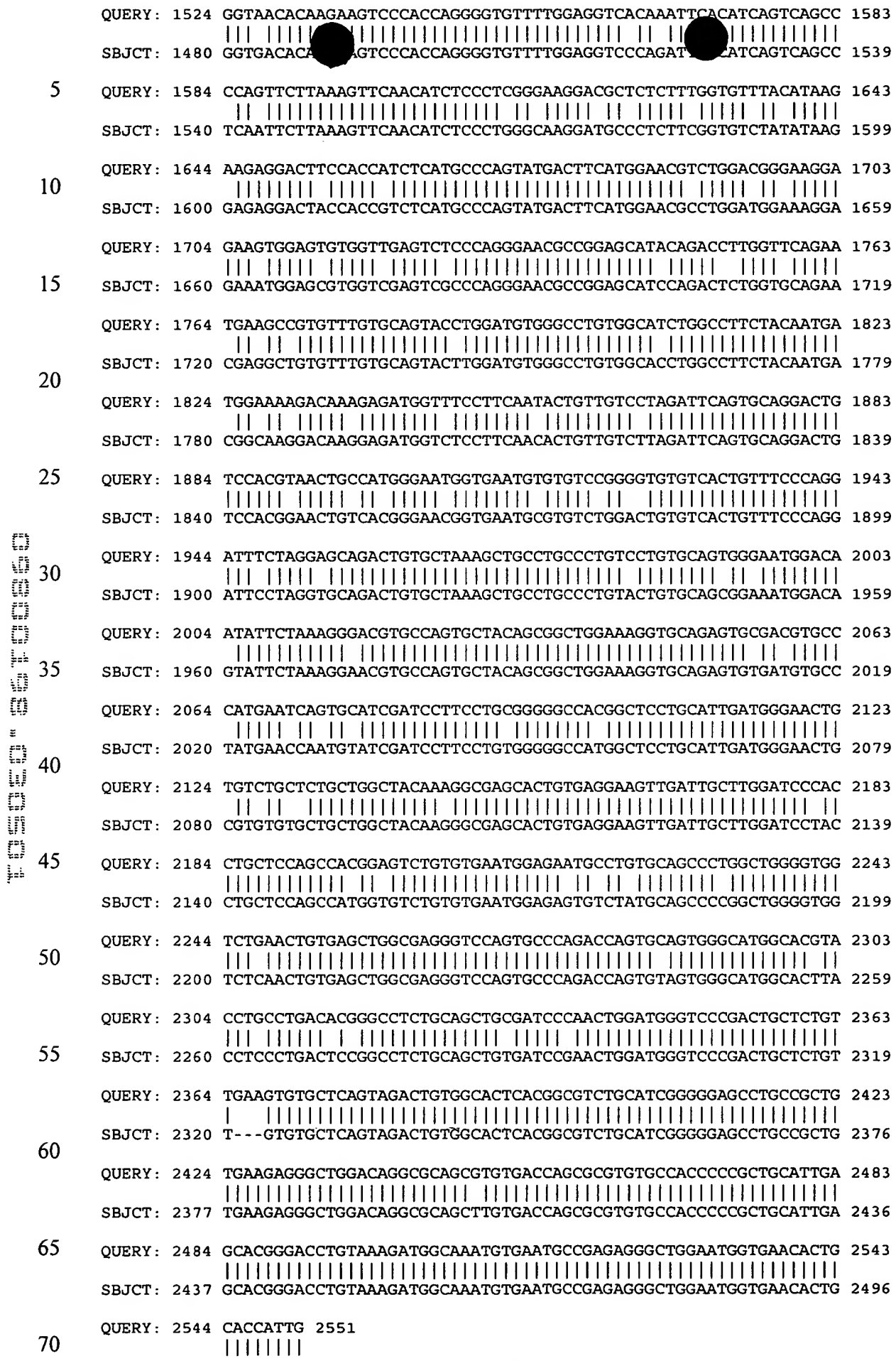
QUERY: 1524 GGTAACACAAGAAGTCCCACCAGGGGTGTTTTGGAGGTCACAAATTCACATCAGTCAGCC 1583
SBJCT: 1480 GGTGACACA[redacted]AGTCCCACCAGGGGTGTTTTGGAGGTCCCAGAT[redacted]CATCAGTCAGCC 1539
QUERY: 1584 CCAGTTCTTAAAGTTCAACATCTCCCTCGGGAAGGACGCTCTCTTTGGTGTTTACATAAG 1643
SBJCT: 1540 TCAATTCTTAAAGTTCAACATCTCCCTGGGCAAGGATGCCCTCTTCGGTGTCTATATAAG 1599
QUERY: 1644 AAGAGGACTTCCACCATCTCATGCCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGA 1703
SBJCT: 1600 GAGAGGACTACCACCGTCTCATGCCCAGTATGACTTCATGGAACGCCTGGATGGAAAGGA 1659
QUERY: 1704 GAAGTGGAGTGTGGTTGAGTCTCCCAGGGAACGCCGGAGCATACAGACCTTGGTTCAGAA 1763
SBJCT: 1660 GAAATGGAGCGTGGTCGAGTCGCCCAGGGAACGCCGGAGCATCCAGACTCTGGTGCAGAA 1719
QUERY: 1764 TGAAGCCGTGTTTGTGCAGTACCTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGA 1823
SBJCT: 1720 CGAGGCTGTGTTTGTGCAGTACTTGGATGTGGGCCTGTGGCACCTGGCCTTCTACAATGA 1779
QUERY: 1824 TGGAAAAGACAAAGAGATGGTTTCCTTCAATACTGTTGTCCTAGATTCAGTGCAGGACTG 1883
SBJCT: 1780 CGGCAAGGACAAGGAGATGGTCTCCTTCAACACTGTTGTCTTAGATTCAGTGCAGGACTG 1839
QUERY: 1884 TCCACGTAACTGCCATGGGAATGGTGAATGTGTGTCCGGGGTGTGTCACTGTTTCCCAGG 1943
SBJCT: 1840 TCCACGGAACTGTCACGGGAACGGTGAATGCGTGTCTGGACTGTGTCACTGTTTCCCAGG 1899
QUERY: 1944 ATTTCTAGGAGCAGACTGTGCTAAAGCTGCCTGCCCTGTCCTGTGCAGTGGGAATGGACA 2003
SBJCT: 1900 ATTCCTAGGTGCAGACTGTGCTAAAGCTGCCTGCCCTGTACTGTGCAGCGGAAATGGACA 1959
QUERY: 2004 ATATTCTAAAGGGACGTGCCAGTGCTACAGCGGCTGGAAAGGTGCAGAGTGCGACGTGCC 2063
SBJCT: 1960 GTATTCTAAAGGAACGTGCCAGTGCTACAGCGGCTGGAAAGGTGCAGAGTGTGATGTGCC 2019
QUERY: 2064 CATGAATCAGTGCATCGATCCTTCCTGCGGGGGCCACGGCTCCTGCATTGATGGGAACTG 2123
SBJCT: 2020 TATGAACCAATGTATCGATCCTTCCTGTGGGGGCCATGGCTCCTGCATTGATGGGAACTG 2079
QUERY: 2124 TGTCTGCTCTGCTGGCTACAAAGGCGAGCACTGTGAGGAAGTTGATTGCTTGGATCCCAC 2183
SBJCT: 2080 CGTGTGTGCTGCTGGCTACAAGGGCGAGCACTGTGAGGAAGTTGATTGCTTGGATCCTAC 2139
QUERY: 2184 CTGCTCCAGCCACGGAGTCTGTGTGAATGGAGAATGCCTGTGCAGCCCTGGCTGGGGTGG 2243
SBJCT: 2140 CTGCTCCAGCCATGGTGTCTGTGTGAATGGAGAGTGTCTATGCAGCCCCGGCTGGGGTGG 2199
QUERY: 2244 TCTGAACTGTGAGCTGGCGAGGGTCCAGTGCCCAGACCAGTGCAGTGGGCATGGCACGTA 2303
SBJCT: 2200 TCTCAACTGTGAGCTGGCGAGGGTCCAGTGCCCAGACCAGTGTAGTGGGCATGGCACTTA 2259
QUERY: 2304 CCTGCCTGACACGGGCCTCTGCAGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCTGT 2363
SBJCT: 2260 CCTCCCTGACTCCGGCCTCTGCAGCTGTGATCCGAACTGGATGGGTCCCGACTGCTCTGT 2319
QUERY: 2364 TGAAGTGTGCTCAGTAGACTGTGGCACTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTG 2423
SBJCT: 2320 T---GTGTGCTCAGTAGACTGTGGCACTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTG 2376
QUERY: 2424 TGAAGAGGGCTGGACAGGCGCAGCGTGTGACCAGCGCGTGTGCCACCCCCGCTGCATTGA 2483
SBJCT: 2377 TGAAGAGGGCTGGACAGGCGCAGCTTGTGACCAGCGCGTGTGCCACCCCCGCTGCATTGA 2436
QUERY: 2484 GCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTG 2543
SBJCT: 2437 GCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTG 2496
QUERY: 2544 CACCATTG 2551
SBJCT:

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SBJCT: 2497 CACCATTG 2504
 SCORE =  105 BITS (     EXPECT = 5E-19
 IDENTITIES = 81/89      , GAPS = 1/89 (1%)
 STRAND = PLUS / PLUS

QUERY: 8711 AACGAATGAATGAACAGACACACACAATGTTCCAAGTTCCCCTAAAATATGACCCACTTG 8770
            |||||| ||||||| | ||||||| |||||| ||||||||||||||||||||||||||
SBJCT: 8655 AACGAACGAATGAAAACACACACAAAATGTTTCAAGTTCCCCTAAAATATGACCCACTTG 8714

QUERY: 8771 TTCTGGGTCT-ACGCAGAAAAGAGACGCA 8798
            ||| ||||||| | ||||||||||||||||
SBJCT: 8715 TTCCGGGTCTAAGGCAGAAAAGAGACGCA 8743

SCORE = 48.1 BITS (24), EXPECT = 0.093
 IDENTITIES = 30/32 (93%)
 STRAND = PLUS / PLUS

QUERY: 475 CACCGGGAGTCAGATGAGTTTCCTAGACAAGG 506
           |||||||||||| ||||||||| ||||||||||
SBJCT: 7   CACCGGGAGTCCGATGAGTTTTCTAGACAAGG 38
```

In this search it was also found that the FCTR3bcd and e nucleic acids had homology to three fragments of *Rattus norvegicus* neurestin alpha. It has 5498 of 6132 bases (89%) identical to bases 2527-8658, 1081 of 1196 bases (90%) identical to bases 123-1318, 996 of 1088 bases (91%) identical to bases 1440-2527 of *Rattus norvegicus* neurestin alpha (GenBank Acc:NM_020088.1) (Table 3N).

Table 3N. BLASTN of FCTR3b, c, d, and e against *Rattus norvegicus* Neurestin alpha mRNA (SEQ ID NO:66)

```
>GI|9910319|REF|NM_020088.1| RATTUS NORVEGICUS NEURESTIN ALPHA (LOC56762), MRNA
          LENGTH = 8689

 SCORE = 7129 BITS (3596), EXPECT = 0.0
 IDENTITIES = 5498/6132 (89%)
 STRAND = PLUS / PLUS

QUERY: 2578 GATGGCTGCCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGTCAGAACAGCTGG 2637
            |||||||||||||| ||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 2527 GATGGCTGCCCTGATTTGTGCAACGGTAACGGGAGATGCACACTGGGTCAGAACAGCTGG 2586

QUERY: 2638 CAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCCGGATGCAACGTTGCCATGGAAACTTCC 2697
            |||||||||||||||||||||||||||||||||||||||||||||||||||||||||| |||
SBJCT: 2587 CAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCCGGATGCAACGTTGCCATGGAAACCTCC 2646

QUERY: 2698 TGTGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGATTGTTTGGACCCTGACTGC 2757
            || ||||||||||||||||||||||||||||||||||||||| ||  ||||||||||||||
SBJCT: 2647 TGCGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGACTGCCTGGACCCTGACTGC 2706

QUERY: 2758 TGCCTGCAGTCAGCCTGTCAGAACAGCCTGCTCTGCCGGGGGTCCCGGGACCCACTGGAC 2817
            ||||| |||||||||||||||||||||||||||||| |||||||| ||||||||  |||||
SBJCT: 2707 TGCCTCCAGTCAGCCTGTCAGAACAGCCTGCTCTGTCGGGGGTCTCGGGACCCCTTGGAC 2766

QUERY: 2818 ATCATTCAGCAGGGCCAGACGGATTGGCCCGCAGTGAAGTCCTTCTATGACCGTATCAAG 2877
            |||||||||||| |||||||| || ||||| || |||||||||||||||| |||||||||
SBJCT: 2767 ATCATTCAGCAAGGCCAGACAGACTGGCCTGCGGTGAAGTCCTTCTATGATCGTATCAAG 2826

QUERY: 2878 CTCTTGGCAGGCAAGGATAGCACCCACATCATTCCTGGAGAGAACCCTTTCAACAGCAGC 2937
            |||||||||||||||| |||||||||||||||||||||| ||||| ||||| ||||||
SBJCT: 2827 CTCTTGGCAGGCAAGGACAGCACCCACATCATTCCTGGAGACAACCCCTTCAATAGCAGC 2886

QUERY: 2938 TTGGTTTCTCTCATCCGAGGCCAAGTAGTAACTACAGATGGAACTCCCCTGGTCGGTGTG 2997
            |||| ||||| |||||||||||||||||| || ||||| || |||||||| ||||||
SBJCT: 2887 CTGGTGTCTCTGATCCGAGGCCAAGTAGTAACCACGGATGGGACCCCCCTGGTGGGTGTG 2946
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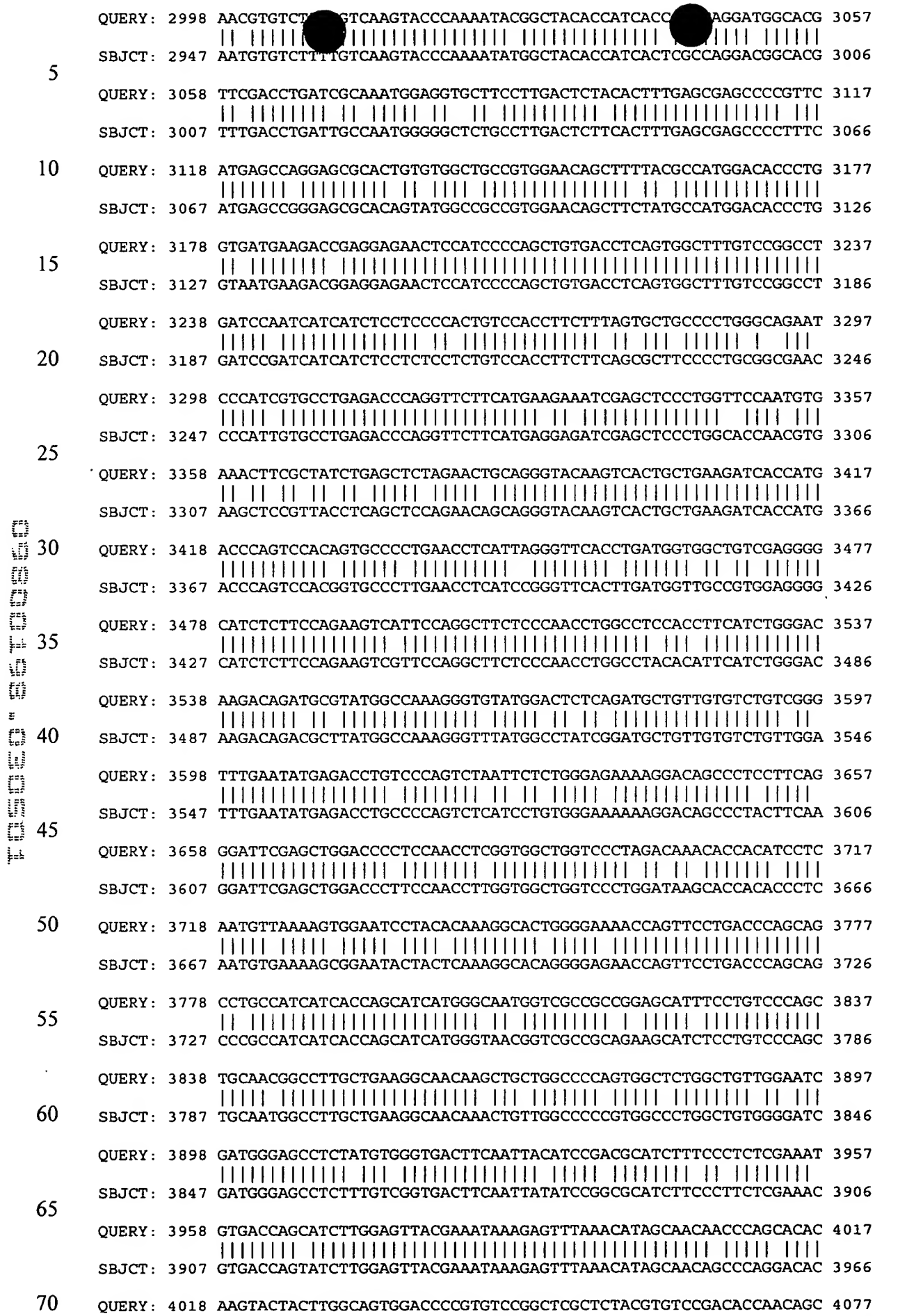
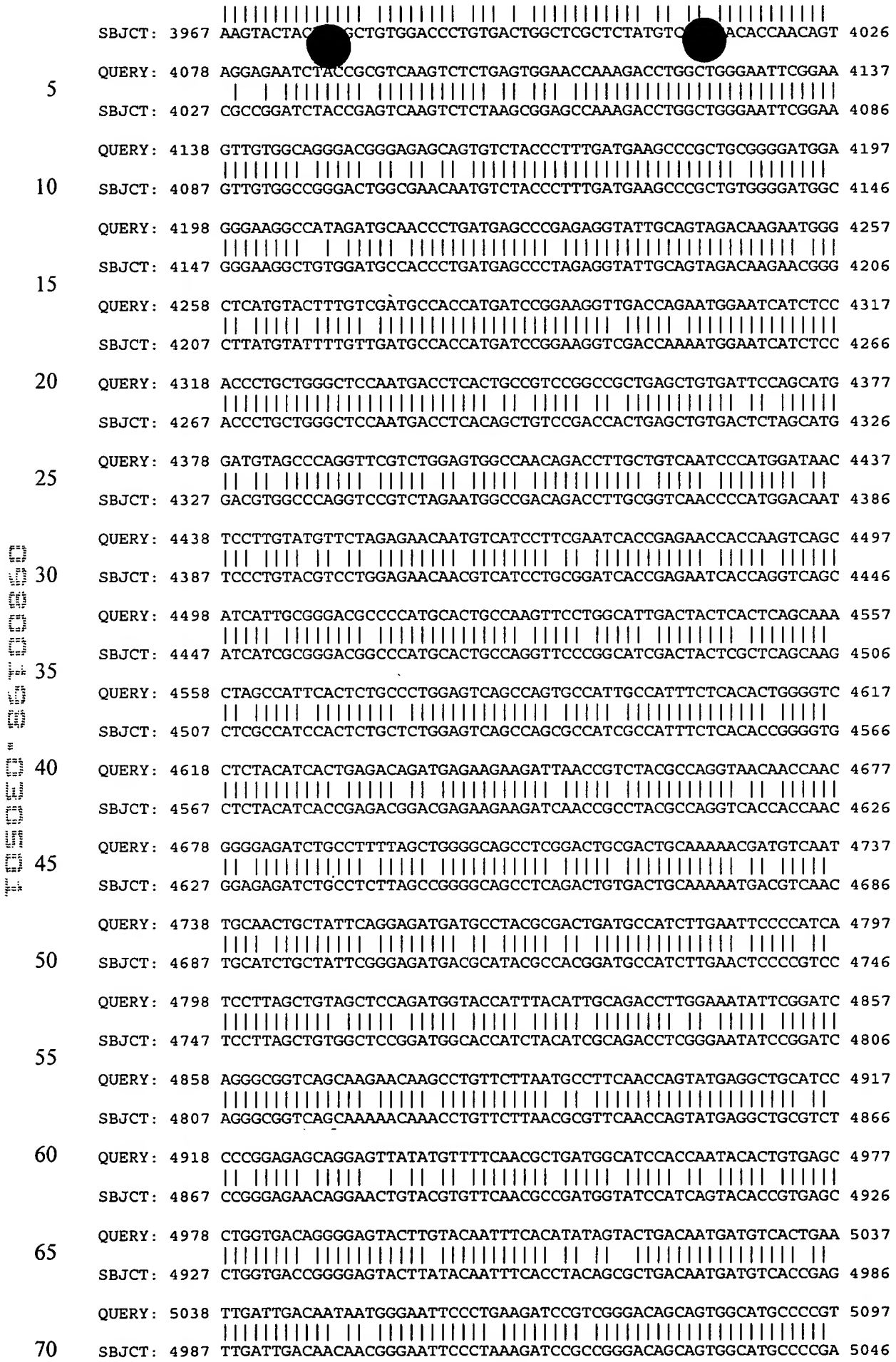

QUERY: 2998 AACGTGTCT GTCAAGTACCCAAAATACGGCTACACCATCACC AGGATGGCACG 3057
SBJCT: 2947 AATGTGTCTTTTGTCAAGTACCCAAAATATGGCTACACCATCACTCGCCAGGACGGCACG 3006
QUERY: 3058 TTCGACCTGATCGCAAATGGAGGTGCTTCCTTGACTCTACACTTTGAGCGAGCCCCGTTC 3117
SBJCT: 3007 TTTGACCTGATTGCCAATGGGGGCTCTGCCTTGACTCTTCACTTTGAGCGAGCCCCTTTC 3066
QUERY: 3118 ATGAGCCAGGAGCGCACTGTGTGGCTGCCGTGGAACAGCTTTTACGCCATGGACACCCTG 3177
SBJCT: 3067 ATGAGCCGGGAGCGCACAGTATGGCCGCCGTGGAACAGCTTCTATGCCATGGACACCCTG 3126
QUERY: 3178 GTGATGAAGACCGAGGAGAACTCCATCCCCAGCTGTGACCTCAGTGGCTTTGTCCGGCCT 3237
SBJCT: 3127 GTAATGAAGACGGAGGAGAACTCCATCCCCAGCTGTGACCTCAGTGGCTTTGTCCGGCCT 3186
QUERY: 3238 GATCCAATCATCATCTCCTCCCCACTGTCCACCTTCTTTAGTGCTGCCCCTGGGCAGAAT 3297
SBJCT: 3187 GATCCGATCATCATCTCCTCTCCTCTGTCCACCTTCTTCAGCGCTTCCCCTGCGGCGAAC 3246
QUERY: 3298 CCCATCGTGCCTGAGACCCAGGTTCTTCATGAAGAAATCGAGCTCCCTGGTTCCAATGTG 3357
SBJCT: 3247 CCCATTGTGCCTGAGACCCAGGTTCTTCATGAGGAGATCGAGCTCCCTGGCACCAACGTG 3306
QUERY: 3358 AAACTTCGCTATCTGAGCTCTAGAACTGCAGGGTACAAGTCACTGCTGAAGATCACCATG 3417
SBJCT: 3307 AAGCTCCGTTACCTCAGCTCCAGAACAGCAGGGTACAAGTCACTGCTGAAGATCACCATG 3366
QUERY: 3418 ACCCAGTCCACAGTGCCCCTGAACCTCATTAGGGTTCACCTGATGGTGGCTGTCGAGGGG 3477
SBJCT: 3367 ACCCAGTCCACGGTGCCCTTGAACCTCATCCGGGTTCACTTGATGGTTGCCGTGGAGGGG 3426
QUERY: 3478 CATCTCTTCCAGAAGTCATTCCAGGCTTCTCCCAACCTGGCCTCCACCTTCATCTGGGAC 3537
SBJCT: 3427 CATCTCTTCCAGAAGTCGTTCCAGGCTTCTCCCAACCTGGCCTACACATTCATCTGGGAC 3486
QUERY: 3538 AAGACAGATGCGTATGGCCAAAGGGTGTATGGACTCTCAGATGCTGTTGTGTCTGTCGGG 3597
SBJCT: 3487 AAGACAGACGCTTATGGCCAAAGGGTTTATGGCCTATCGGATGCTGTTGTGTCTGTTGGA 3546
QUERY: 3598 TTTGAATATGAGACCTGTCCCAGTCTAATTCTCTGGGAGAAAAGGACAGCCCTCCTTCAG 3657
SBJCT: 3547 TTTGAATATGAGACCTGCCCCAGTCTCATCCTGTGGGAAAAAAGGACAGCCCTACTTCAA 3606
QUERY: 3658 GGATTCGAGCTGGACCCCTCCAACCTCGGTGGCTGGTCCCTAGACAAACACCACATCCTC 3717
SBJCT: 3607 GGATTCGAGCTGGACCCTTCCAACCTTGGTGGCTGGTCCCTGGATAAGCACCACACCCTC 3666
QUERY: 3718 AATGTTAAAAGTGGAATCCTACACAAAGGCACTGGGGAAAACCAGTTCCTGACCCAGCAG 3777
SBJCT: 3667 AATGTGAAAAGCGGAATACTACTCAAAGGCACAGGGGAGAACCAGTTCCTGACCCAGCAG 3726
QUERY: 3778 CCTGCCATCATCACCAGCATCATGGGCAATGGTCGCCGCCGGAGCATTTCCTGTCCCAGC 3837
SBJCT: 3727 CCCGCCATCATCACCAGCATCATGGGTAACGGTCGCCGCAGAAGCATCTCCTGTCCCAGC 3786
QUERY: 3838 TGCAACGGCCTTGCTGAAGGCAACAAGCTGCTGGCCCCAGTGGCTCTGGCTGTTGGAATC 3897
SBJCT: 3787 TGCAATGGCCTTGCTGAAGGCAACAAACTGTTGGCCCCCGTGGCCCTGGCTGTGGGGATC 3846
QUERY: 3898 GATGGGAGCCTCTATGTGGGTGACTTCAATTACATCCGACGCATCTTTCCCTCTCGAAAT 3957
SBJCT: 3847 GATGGGAGCCTCTTTGTCGGTGACTTCAATTATATCCGGCGCATCTTCCCTTCTCGAAAC 3906
QUERY: 3958 GTGACCAGCATCTTGGAGTTACGAAATAAAGAGTTTAAACATAGCAACAACCCAGCACAC 4017
SBJCT: 3907 GTGACCAGTATCTTGGAGTTACGAAATAAAGAGTTTAAACATAGCAACAGCCCAGGACAC 3966
QUERY: 4018 AAGTACTACTTGGCAGTGGACCCCGTGTCCGGCTCGCTCTACGTGTCCGACACCAACAGC 4077


SBJCT: 3967 AAGTACTAC GCTGTGGACCCTGTGACTGGCTCGCTCTATGTC ACACCAACAGT 4026
QUERY: 4078 AGGAGAATCTACCGCGTCAAGTCTCTGAGTGGAACCAAAGACCTGGCTGGGAATTCGGAA 4137
SBJCT: 4027 CGCCGGATCTACCGAGTCAAGTCTCTAAGCGGAGCCAAAGACCTGGCTGGGAATTCGGAA 4086
QUERY: 4138 GTTGTGGCAGGGACGGGAGAGCAGTGTCTACCCTTTGATGAAGCCCGCTGCGGGGATGGA 4197
SBJCT: 4087 GTTGTGGCCGGGACTGGCGAACAATGTCTACCCTTTGATGAAGCCCGCTGTGGGGATGGC 4146
QUERY: 4198 GGGAAGGCCATAGATGCAACCCTGATGAGCCCGAGAGGTATTGCAGTAGACAAGAATGGG 4257
SBJCT: 4147 GGGAAGGCTGTGGATGCCACCCTGATGAGCCCTAGAGGTATTGCAGTAGACAAGAACGGG 4206
QUERY: 4258 CTCATGTACTTTGTCGATGCCACCATGATCCGGAAGGTTGACCAGAATGGAATCATCTCC 4317
SBJCT: 4207 CTTATGTATTTTGTTGATGCCACCATGATCCGGAAGGTCGACCAAAATGGAATCATCTCC 4266
QUERY: 4318 ACCCTGCTGGGCTCCAATGACCTCACTGCCGTCCGGCCGCTGAGCTGTGATTCCAGCATG 4377
SBJCT: 4267 ACCCTGCTGGGCTCCAATGACCTCACAGCTGTCCGACCACTGAGCTGTGACTCTAGCATG 4326
QUERY: 4378 GATGTAGCCCAGGTTCGTCTGGAGTGGCCAACAGACCTTGCTGTCAATCCCATGGATAAC 4437
SBJCT: 4327 GACGTGGCCCAGGTCCGTCTAGAATGGCCGACAGACCTTGCGGTCAACCCCATGGACAAT 4386
QUERY: 4438 TCCTTGTATGTTCTAGAGAACAATGTCATCCTTCGAATCACCGAGAACCACCAAGTCAGC 4497
SBJCT: 4387 TCCCTGTACGTCCTGGAGAACAACGTCATCCTGCGGATCACCGAGAATCACCAGGTCAGC 4446
QUERY: 4498 ATCATTGCGGGACGCCCCATGCACTGCCAAGTTCCTGGCATTGACTACTCACTCAGCAAA 4557
SBJCT: 4447 ATCATCGCGGGACGGCCCATGCACTGCCAGGTTCCCGGCATCGACTACTCGCTCAGCAAG 4506
QUERY: 4558 CTAGCCATTCACTCTGCCCTGGAGTCAGCCAGTGCCATTGCCATTTCTCACACTGGGGTC 4617
SBJCT: 4507 CTCGCCATCCACTCTGCTCTGGAGTCAGCCAGCGCCATCGCCATTTCTCACACCGGGGTG 4566
QUERY: 4618 CTCTACATCACTGAGACAGATGAGAAGAAGATTAACCGTCTACGCCAGGTAACAACCAAC 4677
SBJCT: 4567 CTCTACATCACCGAGACGGACGAGAAGAAGATCAACCGCCTACGCCAGGTCACCACCAAC 4626
QUERY: 4678 GGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCGACTGCAAAAACGATGTCAAT 4737
SBJCT: 4627 GGAGAGATCTGCCTCTTAGCCGGGGCAGCCTCAGACTGTGACTGCAAAAATGACGTCAAC 4686
QUERY: 4738 TGCAACTGCTATTCAGGAGATGATGCCTACGCGACTGATGCCATCTTGAATTCCCCATCA 4797
SBJCT: 4687 TGCATCTGCTATTCGGGAGATGACGCATACGCCACGGATGCCATCTTGAACTCCCCGTCC 4746
QUERY: 4798 TCCTTAGCTGTAGCTCCAGATGGTACCATTTACATTGCAGACCTTGGAAATATTCGGATC 4857
SBJCT: 4747 TCCTTAGCTGTGGCTCCGGATGGCACCATCTACATCGCAGACCTCGGGAATATCCGGATC 4806
QUERY: 4858 AGGGCGGTCAGCAAGAACAAGCCTGTTCTTAATGCCTTCAACCAGTATGAGGCTGCATCC 4917
SBJCT: 4807 AGGGCGGTCAGCAAAAACAAACCTGTTCTTAACGCGTTCAACCAGTATGAGGCTGCGTCT 4866
QUERY: 4918 CCCGGAGAGCAGGAGTTATATGTTTTCAACGCTGATGGCATCCACCAATACACTGTGAGC 4977
SBJCT: 4867 CCGGGAGAACAGGAACTGTACGTGTTCAACGCCGATGGTATCCATCAGTACACCGTGAGC 4926
QUERY: 4978 CTGGTGACAGGGGAGTACTTGTACAATTTCACATATAGTACTGACAATGATGTCACTGAA 5037
SBJCT: 4927 CTGGTGACCGGGGAGTACTTATACAATTTCACCTACAGCGCTGACAATGATGTCACCGAG 4986
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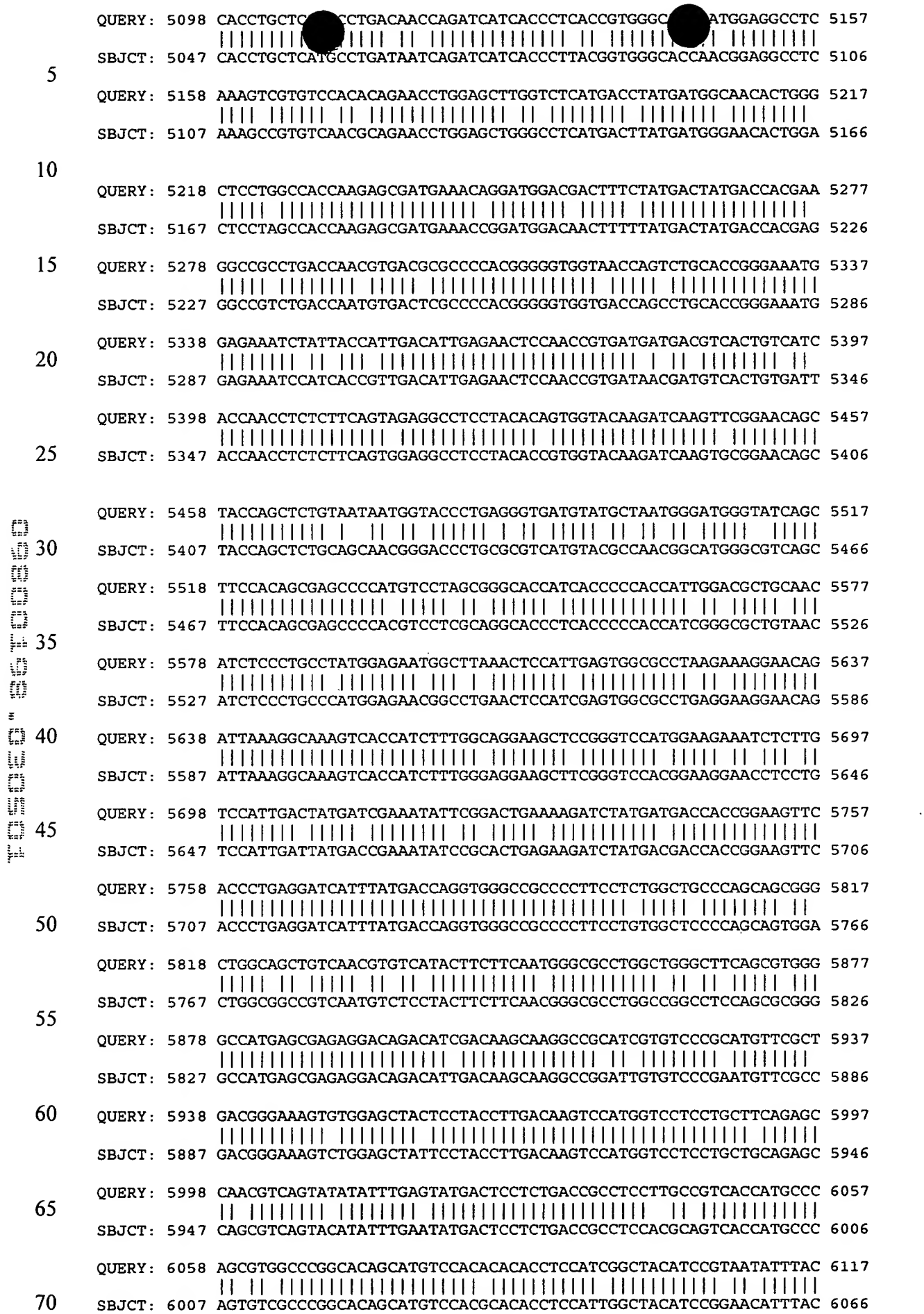
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SBJCT: 5827 GCCATGAGCGAGAGGACAGACATTGACAAGCAAGGCCGGATTGTGTCCCGAATGTTCGCC 5886
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QUERY: 6058 AGCGTGGCCCGGCACAGCATGTCCACACACACCTCCATCGGCTACATCCGTAATATTTAC 6117
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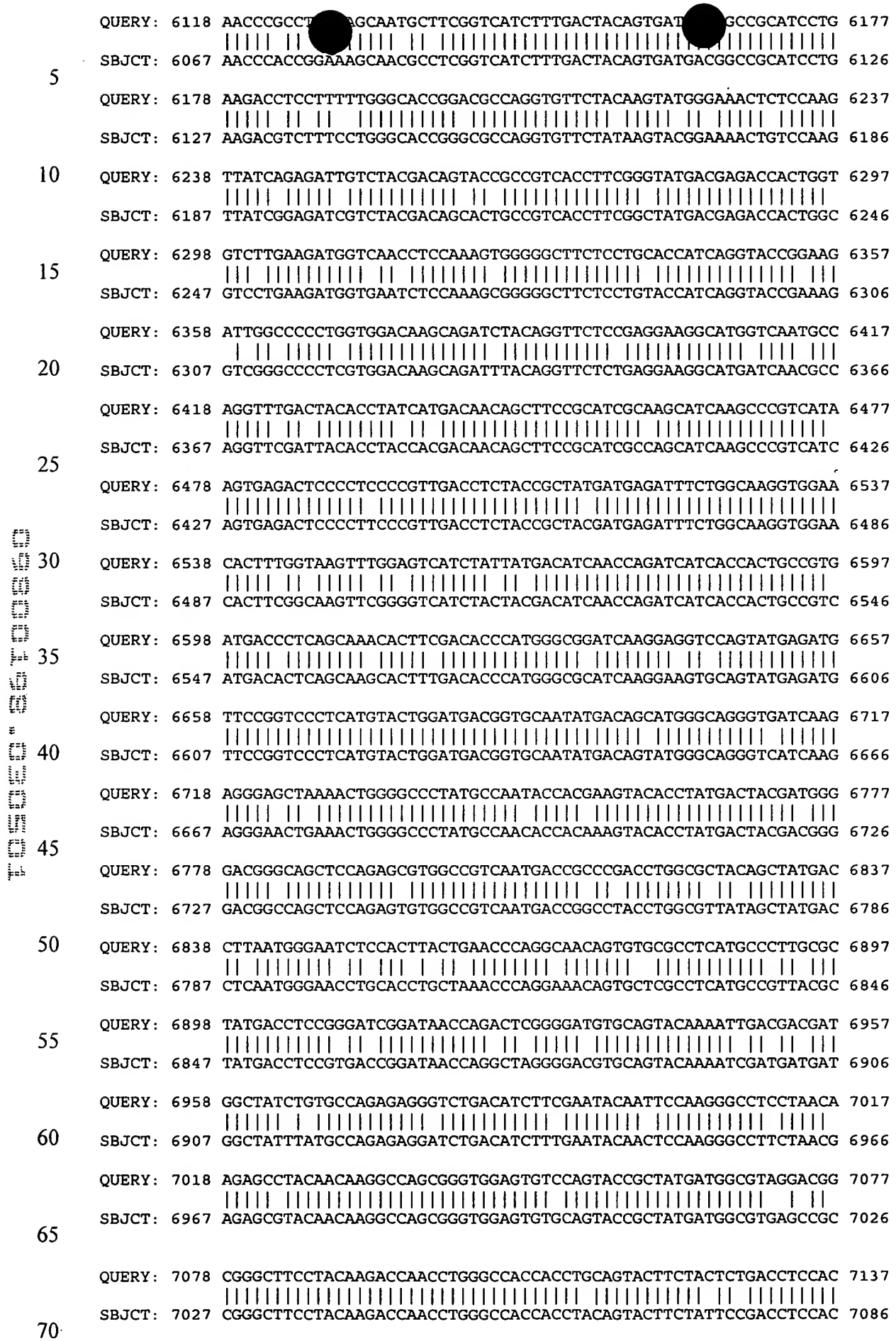
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SBJCT: 6187 TTATCGGAGATCGTCTACGACAGCACTGCCGTCACCTTCGGCTATGACGAGACCACTGGC 6246
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QUERY: 6358 ATTGGCCCCCTGGTGGACAAGCAGATCTACAGGTTCTCCGAGGAAGGCATGGTCAATGCC 6417
SBJCT: 6307 GTCGGGCCCCTCGTGGACAAGCAGATTTACAGGTTCTCTGAGGAAGGCATGATCAACGCC 6366
QUERY: 6418 AGGTTTGACTACACCTATCATGACAACAGCTTCCGCATCGCAAGCATCAAGCCCGTCATA 6477
SBJCT: 6367 AGGTTCGATTACACCTACCACGACAACAGCTTCCGCATCGCCAGCATCAAGCCCGTCATC 6426
QUERY: 6478 AGTGAGACTCCCCTCCCCGTTGACCTCTACCGCTATGATGAGATTTCTGGCAAGGTGGAA 6537
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SBJCT: 6487 CACTTCGGCAAGTTCGGGGTCATCTACTACGACATCAACCAGATCATCACCACTGCCGTC 6546
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QUERY: 6718 AGGGAGCTAAAACTGGGGCCCTATGCCAATACCACGAAGTACACCTATGACTACGATGGG 6777
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QUERY: 6778 GACGGGCAGCTCCAGAGCGTGGCCGTCAATGACCGCCCGACCTGGCGCTACAGCTATGAC 6837
SBJCT: 6727 GACGGCCAGCTCCAGAGTGTGGCCGTCAATGACCGGCCTACCTGGCGTTATAGCTATGAC 6786
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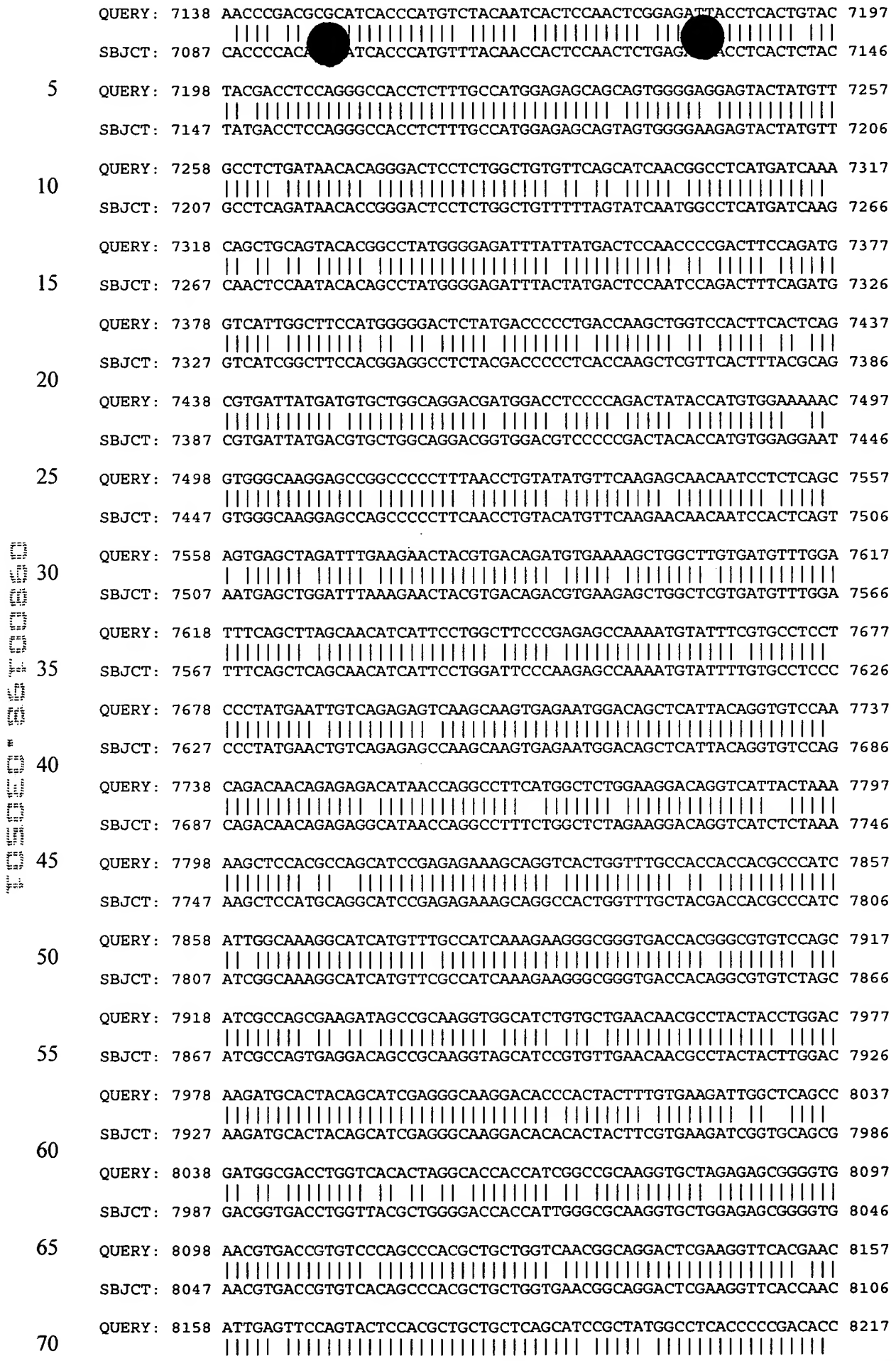
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SBJCT: 7447 GTGGGCAAGGAGCCAGCCCCCTTCAACCTGTACATGTTCAAGAACAACAATCCACTCAGT 7506
QUERY: 7558 AGTGAGCTAGATTTGAAGAACTACGTGACAGATGTGAAAAGCTGGCTTGTGATGTTTGGA 7617
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QUERY: 7618 TTTCAGCTTAGCAACATCATTCCTGGCTTCCCGAGAGCCAAAATGTATTTCGTGCCTCCT 7677
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QUERY: 8278 TGGGCCAAGGAGCAGCAGAAAGCCAGGGACGGGAGAGAGGGGAGCCGCCTGTGGACTGAG 8337
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QUERY: 8338 GGCGAGAAGCAGCAGCTTCTGAGCACCGGGCGCGTGCAAGGGTACGAGGGATATTACGTG 8397
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QUERY: 8458 CAGAATGAGATGGGAAAGAGGTAACAAAATAATCTGCTGCCATTCCTTGTCTGAATGGCT 8517
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QUERY: 8518 CAGCAGGAGTAACTGTTATCTCCTCTCCTAAGGAGATGAAGACCTAACAGGGGCACTGCG 8577
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SBJCT: 8467 CAGCAGGAGCAACTGTGACCTCCTCTCCTAAGGAGACGAAGACCTAACAGGGGCACTGAG 8526

QUERY: 8578 GCTGGGCTGCTTTAGGAGACCAAGTGGCAAGAAAGCTCACATTTTTTGAGTTCAAATGCT 8637
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SBJCT: 8527 GCCGGGCTGCTTTAGGACCCCAAGTGGCAAGAAAGCTCACATTTTTTGAGTTCAAATGCT 8586

QUERY: 8638 ACTGTCCAAGCGAGAAGTCCCTCATCCTGAAGTAGACTAAAGCCCGGCTGAAAATTCCGA 8697
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QUERY: 8698 GGAAAACAAAAC 8709
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SBJCT: 8647 GGAAAACAAAAC 8658

SCORE = 1459 BITS (736), EXPECT = 0.0
 IDENTITIES = 1081/1196 (90%)
 STRAND = PLUS / PLUS

QUERY: 270  ATCTGGAATAATGGATGTAAAGGACCGGCGACACCGCTCTTTGACCAGAGGACGCTGTGG 329
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SBJCT: 123  ATCTGCAATAATGGATGTGAAGGATCGGCGACATCGCTCTTTGACCAGGGGACGGTGTGG 182

QUERY: 330  CAAAGAGTGTCGCTACACAAGCTCCTCTCTGGACAGTGAGGACTGCCGGGTGCCCACACA 389
           ||| |||||||||||||| |||||||||||||||||||||||||||| |||||||| ||
SBJCT: 183  CAAGGAGTGTCGCTACACCAGCTCCTCTCTGGACAGTGAGGACTGCCGTGTGCCCACGCA 242

QUERY: 390  GAAATCCTACAGCTCCAGTGAGACTCTGAAGGCCTATGACCATGACAGCAGGATGCACTA 449
           ||| |||||||| |||||||||| |||||||| |||||||||||||||| |||||||||
SBJCT: 243  GAAGTCCTACAGTTCCAGTGAGACCCTGAAGGCTTATGACCATGACAGCAGAATGCACTA 302

QUERY: 450  TGGAAACCGAGTCACAGACCTCATCCACCGGGAGTCAGATGAGTTTCCTAGACAAGGAAC 509
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SBJCT: 303  TGGAAACCGAGTCACAGACCTGGTGCACCGGGAGTCCGATGAGTTTTCTAGACAAGGGGC 362

QUERY: 510  CAACTTCACCCTTGCCGAACTGGGCATCTGTGAGCCCTCCCCACACCGAAGCGGCTACTG 569
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SBJCT: 363  TAATTTCACCCTGGCAGAATTGGGAATCTGCGAGCCCTCCCCACACCGAAGTGGTTACTG 422

QUERY: 570  CTCCGACATGGGGATCCTTCACCAGGGCTACTCCCTTAGCACAGGGTCTGACGCCGACTC 629
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SBJCT: 423  TTCCGACATGGGGATCCTCCACCAGGGCTACTCCCTGAGCACTGGGTCTGATGCGGACTC 482

QUERY: 630  CGACACCGAGGGAGGGATGTCTCCAGAACACGCCATCAGACTGTGGGGCAGAGGGATAAA 689
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QUERY: 690  ATCCAGGCGCAGTTCCGGCCTGTCCAGTCGTGAAAACTCGGCCCTTACCCTGACTGACTC 749
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SBJCT: 543  ATCGAGGCG  TCTGGCTTGTCCAGCCGCGAGAACTCAGCCCT  CTGACTGATTC 602

QUERY: 750  TGACAACGAAAACAAATCAGATGATGAGAACGGTCGTCCCATTCCACCTACATCCTCGCC 809
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SBJCT: 603  TGACAATGAAAATAAATCGGATGACGACAATGGTCGACCCATTCCACCTACATCCTCGTC 662

QUERY: 810  TAGTCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATAATCCTCCACCAGTTAGCTGCCA 869
            |||  ||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 663  TAGCCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATAATCCTCCACCAGTTAGCTGCCA 722

QUERY: 870  GATGCCATTGCTAGACAGCAACACCTCCCATCAAATCATGGACACCAACCCTGATGAGGA 929
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QUERY: 930  ATTCTCCCCCAATTCATACCTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGCAG 989
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SBJCT: 783  ATTCTCCCCTAATTCATACCTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGTAG 842

QUERY: 990  TGGCCCTCCGAACCACCACAGCCAGTCGACTCTGAGGCCCCCTCTCCCACCCCCTCACAA 1049
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QUERY: 1050 CCACACGCTGTCCCATCACCACTCGTCCGCCAACTCCCTCAACAGGAACTCACTGACCAA 1109
            ||||||  ||||||||  ||||||||  ||  ||||||||||||||||  ||||||||||||||
SBJCT: 903  CCACACCCTGTCCCACCACCACTCCTCTGCCAACTCCCTCAACAGAAACTCACTGACCAA 962

QUERY: 1110 TCGGCGGAGTCAGATCCACGCCCCGGCCCCAGCGCCCAATGACCTGGCCACCACACCAGA 1169
            ||||||||||||  ||||||||||||  ||  ||  ||  ||||||||||||||||||||  ||  ||
SBJCT: 963  TCGGCGGAGTCAAATCCACGCCCCAGCTCCTGCACCCAATGACCTGGCCACCACGCCGGA 1022

QUERY: 1170 GTCCGTTCAGCTTCAGGACAGCTGGGTGCTAAACAGCAACGTGCCACTGGAGACCCGGCA 1229
            ||||||||||||  ||||||||||||||||||  |||||  ||||||||  ||||||||  |||||
SBJCT: 1023 GTCCGTTCAGCTCCAGGACAGCTGGGTGCTGAACAGTAACGTGCCGCTGGAGACGCGGCA 1082

QUERY: 1230 CTTCCTCTTCAAGACCTCCTCGGGGAGCACACCCTTGTTCAGCAGCTCTTCCCCGGGATA 1289
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SBJCT: 1083 CTTCCTCTTCAAGACGTCCTCCGGAAGCACACCCCTGTTCAGCAGCTCTTCTCCAGGATA 1142

QUERY: 1290 CCCTTTGACCTCAGGAACGGTTTACACGCCCCCGCCCCGCCTGCTGCCCAGGAATACTTT 1349
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QUERY: 1350 CTCCAGGAAGGCTTTCAAGCTGAAGAAGCCCTCCAAATACTGCAGCTGGAAATGTGCTGC 1409
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SBJCT: 1203 CTCTAGGAAGGCCTTCAAGCTGAAGAAACCCTCCAAATACTGCAGTTGGAAATGCGCCGC 1262

QUERY: 1410 CCTCTCCGCCATTGCCGCGGCCCTCCTCTTGGCTATTTTGCTGGCGTATTTCATAG 1465
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SBJCT: 1263 CCTGTCTGCCATTGCCGCTGCCCTCCTTCTGGCCATTTTGCTGGCCTATTTCATAG 1318

SCORE = 1427 BITS (720), EXPECT = 0.0
 IDENTITIES = 996/1088 (91%)
 STRAND = PLUS / PLUS

QUERY: 1464 AGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCG 1523
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SBJCT: 1440 AGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGCGGCGAGGCAGAAGTCGGTCGACG 1499

QUERY: 1524 GGTAACACAAGAAGTCCCACCAGGGGTGTTTTGGAGGTCACAAATTCACATCAGTCAGCC 1583
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SBJCT: 1500 GGTGACACAGGAAGTCCCACCAGGGGTGTTTTGGAGGTCCCAGATTCACATCAGTCAGCC 1559

QUERY: 1584 CCAGTTCTTAAAGTTCAACATCTCCCTCGGGAAGGACGCTCTCTTTGGTGTTTACATAAG 1643
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QUERY: 1644 AAGAGGACTTCCACCATCTCATGCCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGA 1703
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SBJCT: 1620 AAGAGGACTGCCACCATCTCATGCACAGTATGACTTCATGGAACGCCTGGACGGAAAGGA 1679

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           |||||||||||||||| ||||| |||||||||||||||||||| |||||| |||| |||||
SBJCT: 1680 GAAGTGGAGTGTGGTCGAGTCACCCAGGGAACGCCGGAGCATCCAGACCCTGGTGCAGAA 1739

QUERY: 1764 TGAAGCCGTGTTTGTGCAGTACCTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGA 1823
           || || ||||| ||||||||| |||||||||||||||||||| || ||||||||||||||
SBJCT: 1740 CGAGGCTGTGTTCGTGCAGTACTTGGATGTGGGCCTGTGGCACCTCGCCTTCTACAATGA 1799

QUERY: 1824 TGGAAAAGACAAAGAGATGGTTTCCTTCAATACTGTTGTCCTAGATTCAGTGCAGGACTG 1883
           || || ||||| |||||||| |||||||||| |||||| ||||||||||||||||||||
SBJCT: 1800 CGGCAAGGACAAGGAGATGGTCTCCTTCAATACGGTTGTCTTAGATTCAGTGCAGGACTG 1859

QUERY: 1884 TCCACGTAACTGCCATGGGAATGGTGAATGTGTGTCCGGGGTGTGTCACTGTTTCCCAGG 1943
           |||||| |||||||| ||||| || ||||| ||||| ||  ||||||||||||||||||
SBJCT: 1860 TCCACGAAACTGCCACGGGAACGGCGAATGCGTGTCTGGACTGTGTCACTGTTTCCCAGG 1919

QUERY: 1944 ATTTCTAGGAGCAGACTGTGCTAAAGCTGCCTGCCCTGTCCTGTGCAGTGGGAATGGACA 2003
           ||| ||||| |||||||| |||||||||||||||||||| ||||||||||||||||||||
SBJCT: 1920 ATTCCTAGGTGCAGACTGCGCTAAAGCTGCCTGCCCTGTTCTGTGCAGTGGGAATGGACA 1979

QUERY: 2004 ATATTCTAAAGGGACGTGCCAGTGCTACAGCGGCTGGAAAGGTGCAGAGTGCGACGTGCC 2063
           ||||| |||||||| |||||||||||| |||||||||| ||||| ||||| |||||
SBJCT: 1980 GTATTCCAAAGGGACATGCCAGTGCTACAGTGGCTGGAAAGGAGCAGAATGCGATGTGCC 2039

QUERY: 2064 CATGAATCAGTGCATCGATCCTTCCTGCGGGGGCCACGGCTCCTGCATTGATGGGAACTG 2123
           |||||| |||||||||||||||||||| ||||||||||||||||||||||||||||||
SBJCT: 2040 CATGAACCAGTGCATCGATCCTTCCTGTGGGGGCCACGGCTCCTGCATTGATGGGAACTG 2099

QUERY: 2124 TGTCTGCTCTGCTGGCTACAAAGGCGAGCACTGTGAGGAAGTTGATTGCTTGGATCCCAC 2183
           || ||  | |||||||||| |||||||||| || ||||| |||||||||||||| ||
SBJCT: 2100 CGTGTGTGCAGCTGGCTACAAGGGCGAGCACTGCGAAGAAGTGGATTGCTTGGATCCAAC 2159

QUERY: 2184 CTGCTCCAGCCACGGAGTCTGTGTGAATGGAGAATGCCTGTGCAGCCCTGGCTGGGGTGG 2243
           |||||||||||| || |||||||||| ||||| || || |||||||| |||||||| ||
SBJCT: 2160 CTGCTCCAGCCATGGTGTCTGTGTGAACGGAGAGTGTCTATGCAGCCCCGGCTGGGGCGG 2219

QUERY: 2244 TCTGAACTGTGAGCTGGCGAGGGTCCAGTGCCCAGACCAGTGCAGTGGGCATGGCACGTA 2303
           || ||||| |||||||||||||||||||||||||||||| ||||||||||||||| ||
SBJCT: 2220 GCTCAACTGCGAGCTGGCGAGGGTCCAGTGCCCAGACCAGTGTAGTGGGCATGGCACTTA 2279

QUERY: 2304 CCTGCCTGACACGGGCCTCTGCAGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCTGT 2363
           ||| |||||| | |||||||||| ||| ||||| || ||||||||||||||||||||||
SBJCT: 2280 CCTCCCTGACTCTGGCCTCTGCAACTGTGATCCGAATTGGATGGGTCCCGACTGCTCTGT 2339

QUERY: 2364 TGAAGTGTGCTCAGTAGACTGTGGCACTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTG 2423
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 2340 TGAAGTGTGCTCAGTAGACTGTGGCACTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTG 2399

QUERY: 2424 TGAAGAGGGCTGGACAGGCGCAGCGTGTGACCAGCGCGTGTGCCACCCCCGCTGCATTGA 2483
           |||||||||||||||||||| || ||||||||||||||||||||||||||||||||||||
SBJCT: 2400 TGAAGAGGGCTGGACAGGCGCGGCTTGTGACCAGCGCGTGTGCCACCCCCGCTGCATTGA 2459

QUERY: 2484 GCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTG 2543
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 2460 GCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTG 2519

QUERY: 2544 CACCATTG 2551
           ||||||||
SBJCT: 2520 CACCATTG 2527
```

In this search it was also found that the FCTR3bcd and e nucleic acid had homology to six fragments of *Gallus gallus* partial mRNA for teneurin-2. It has 2780 of 3449 bases (80%) identical to bases 3386-6834, 1553 of 1862 bases (83%) identical to bases 1414-3275, 540 of

628 bases (85%) identical to bases 587-1214, 593 of 725 bases (81%) identical to bases 7084-7808, 429 of 515 bases (83%) identical to bases 7895-8409, and 397 of 475 bases (83%) identical to bases 20-494 of *Gallus gallus* partial mRNA for teneurin-2. (EMBL Acc: GGA278031) (Table 3O).

Table 3O. BLASTN of FCTR3b, c, d, and e against *Gallus gallus* Teneurin-2 mRNA (SEQ ID NO:67)

```
>GI|10241573|EMB|AJ279031.1|GGA279031 GALLUS GALLUS PARTIAL MRNA FOR TENEURIN-2 (TEN2
GENE), LONG SPLICE
           VARIANT
         LENGTH = 8409

 SCORE = 1532 BITS (773), EXPECT = 0.0
 IDENTITIES = 2780/3449 (80%)
 STRAND = PLUS / PLUS

QUERY: 3458 TGATGGTGGCTGTCGAGGGGCATCTCTTCCAGAAGTCATTCCAGGCTTCTCCCAACCTGG 3517
           ||||||| || || || |||||||| || || || ||||| | ||| ||||||||| |||
SBJCT: 3386 TGATGGTAGCAGTAGAAGGGCATCTATTTCAAAAATCATTTCTGGCATCTCCCAACTTGG 3445

QUERY: 3518 CCTCCACCTTCATCTGGGACAAGACAGATGCGTATGGCCAAAGGGTGTATGGACTCTCAG 3577
           | |  || |||||||||||||| |||||||| ||||| || | ||| |||||  | ||||
SBJCT: 3446 CTTATACATTCATCTGGGACAAAACAGATGCATATGGTCAGAAGGTTTATGGGTTGTCAG 3505

QUERY: 3578 ATGCTGTTGTGTCTGTCGGGTTTGAATATGAGACCTGTCCCAGTCTAATTCTCTGGGAGA 3637
           ||||||| || ||||| || |||||||||||||| ||||||||| | ||||| |||||||
SBJCT: 3506 ATGCTGTAGTTTCTGTGGGTTTTGAATATGAGACTTGTCCCAGTTTGATTCTGTGGGAGA 3565

QUERY: 3638 AAAGGACAGCCCTCCTTCAGGGATTCGAGCTGGACCCCTCCAACCTCGGTGGCTGGTCCC 3697
           ||||||| || || || || ||||| ||||| || || ||||| || || || |||||
SBJCT: 3566 AAAGGACTGCGCTGCTGCAAGGATTTGAGCTAGATCCTTCCAATCTAGGAGGATGGTCTT 3625

QUERY: 3698 TAGACAAACACCACATCCTCAATGTTAAAAGTGGAATCCTACACAAAGGCACTGGGGAAA 3757
           | || ||||| ||  | || ||||| || ||||| ||  | |||||||||| ||| ||||
SBJCT: 3626 TGGATAAACATCATGTACTGAATGTCAAGAGTGGTATATTGCACAAAGGCAATGGAGAAA 3685

QUERY: 3758 ACCAGTTCCTGACCCAGCAGCCTGCCATCATCACCAGCATCATGGGCAATGGTCGCCGCC 3817
           | ||||| || || |||||||| ||  | || |||||||| ||||| ||||| |||||
SBJCT: 3686 ATCAGTTTCTAACTCAGCAGCCAGCTGTGATAACCAGCATTATGGGGAATGGGCGCCGAA 3745

QUERY: 3818 GGAGCATTTCCTGTCCCAGCTGCAACGGCCTTGCTGAAGGCAACAAGCTGCTGGCCCCAG 3877
           | ||||| |||||||| |||||||| || ||||| ||||| || ||||| ||||||| |
SBJCT: 3746 GAAGCATATCCTGTCCTAGCTGCAATGGTCTTGCAGAAGGAAATAAGCTTTTGGCCCCTG 3805

QUERY: 3878 TGGCTCTGGCTGTTGGAATCGATGGGAGCCTCTATGTGGGTGACTTCAATTACATCCGAC 3937
           | || ||||| || ||||| ||||| ||||||| ||| || || || |||||||| || |
SBJCT: 3806 TAGCACTGGCAGTGGGAATTGATGGAAGCCTCTTTGTTGGAGATTTTAATTACATTCGGC 3865

QUERY: 3938 GCATCTTTCCCTCTCGAAATGTGACCAGCATCTTGGAGTTACGAAATAAAGAGTTTAAAC 3997
           | ||||| || ||  | |||||||| ||||| |||||| |  ||||||||||||||||||
SBJCT: 3866 GTATCTTCCCATCCAGGAATGTGACTAGCATATTGGAGCTGAGAAATAAAGAGTTTAAAC 3925

QUERY: 3998 ATAGCAACAACCCAGCACACAAGTACTACTTGGCAGTGGACCCCGTGTCCGGCTCGCTCT 4057
           |||||||||| || || ||||| |||||  |||| |||||||||| || ||||| || |
SBJCT: 3926 ATAGCAACAATCCTGCTCACAAATACTATCTGGCCGTGGACCCCGTTTCGGGCTCCCTGT 3985

QUERY: 4058 ACGTGTCCGACACCAACAGCAGGAGAATCTACCGCGTCAAGTCTCTGAGTGGAACCAAAG 4117
           |||| || |||||||||||| |  | || |||  ||||| ||||| | ||| || ||||
SBJCT: 3986 ACGTATCAGACACCAACAGCCGACGGATATACAAAGTCAAATCTCTTACTGGCACGAAAG 4045

QUERY: 4118 ACCTGGCTGGGAATTCGGAAGTTGTGGCAGGGACGGGAGAGCAGTGTCTACCCTTTGATG 4177
           |||||||||| ||||| ||||| || || ||||| |||||||| || || ||||||||||
SBJCT: 4046 ACCTGGCTGGTAATTCTGAAGTGGTAGCGGGGACTGGAGAGCAATGCCTGCCCTTTGATG 4105
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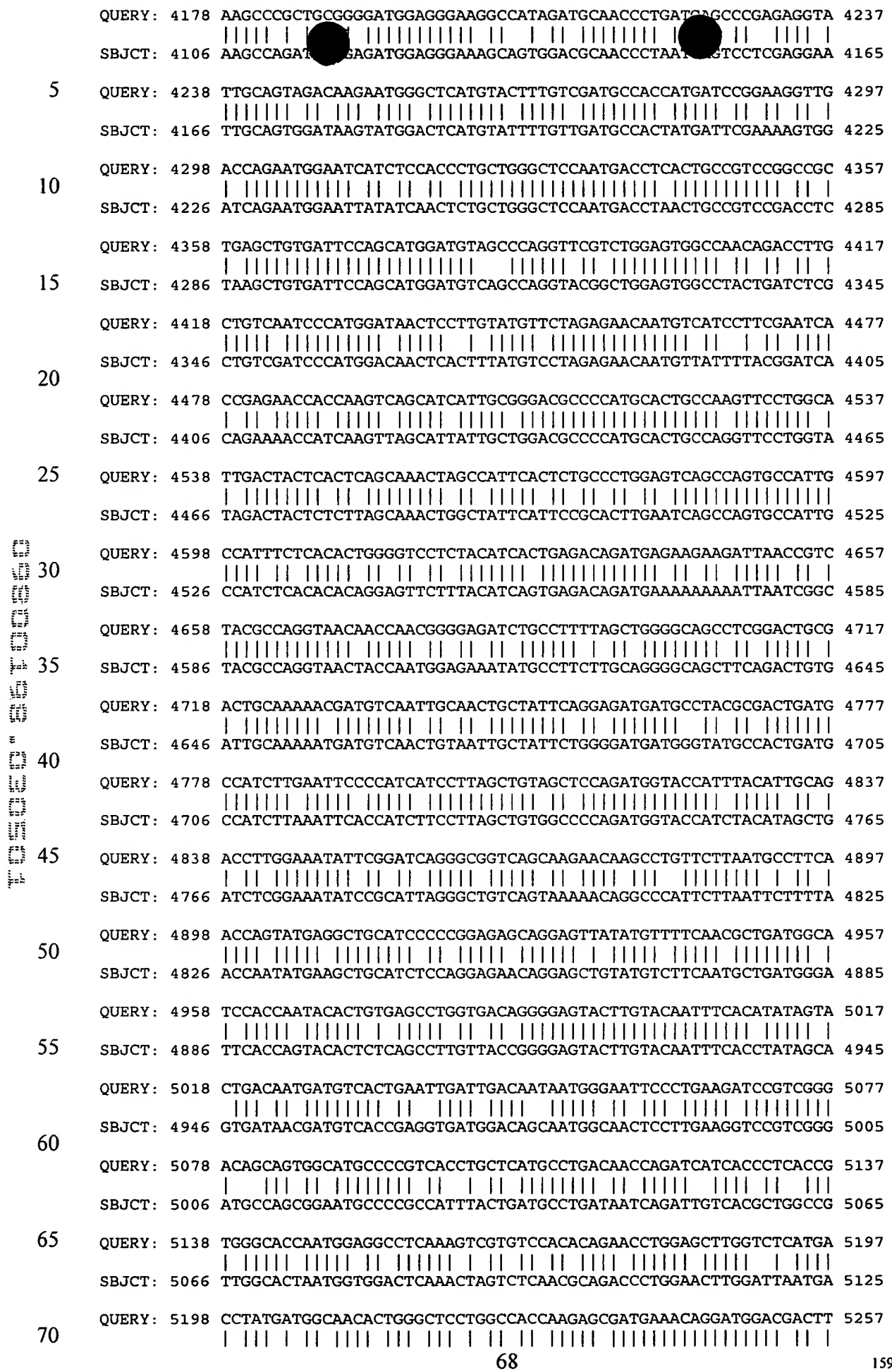
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QUERY: 4238 TTGCAGTAGACAAGAATGGGCTCATGTACTTTGTCGATGCCACCATGATCCGGAAGGTTG 4297
SBJCT: 4166 TTGCAGTGGATAAGTATGGACTCATGTATTTTGTTGATGCCACTATGATTCGAAAAGTGG 4225
QUERY: 4298 ACCAGAATGGAATCATCTCCACCCTGCTGGGCTCCAATGACCTCACTGCCGTCCGGCCGC 4357
SBJCT: 4226 ATCAGAATGGAATTATATCAACTCTGCTGGGCTCCAATGACCTAACTGCCGTCCGACCTC 4285
QUERY: 4358 TGAGCTGTGATTCCAGCATGGATGTAGCCCAGGTTCGTCTGGAGTGGCCAACAGACCTTG 4417
SBJCT: 4286 TAAGCTGTGATTCCAGCATGGATGTCAGCCAGGTACGGCTGGAGTGGCCTACTGATCTCG 4345
QUERY: 4418 CTGTCAATCCCATGGATAACTCCTTGTATGTTCTAGAGAACAATGTCATCCTTCGAATCA 4477
SBJCT: 4346 CTGTCGATCCCATGGACAACTCACTTTATGTCCTAGAGAACAATGTTATTTTACGGATCA 4405
QUERY: 4478 CCGAGAACCACCAAGTCAGCATCATTGCGGGACGCCCCATGCACTGCCAAGTTCCTGGCA 4537
SBJCT: 4406 CAGAAAACCATCAAGTTAGCATTATTGCTGGACGCCCCATGCACTGCCAGGTTCCTGGTA 4465
QUERY: 4538 TTGACTACTCACTCAGCAAACTAGCCATTCACTCTGCCCTGGAGTCAGCCAGTGCCATTG 4597
SBJCT: 4466 TAGACTACTCTCTTAGCAAACTGGCTATTCATTCCGCACTTGAATCAGCCAGTGCCATTG 4525
QUERY: 4598 CCATTTCTCACACTGGGGTCCTCTACATCACTGAGACAGATGAGAAGAAGATTAACCGTC 4657
SBJCT: 4526 CCATCTCACACACAGGAGTTCTTTACATCAGTGAGACAGATGAAAAAAAAATTAATCGGC 4585
QUERY: 4658 TACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCG 4717
SBJCT: 4586 TACGCCAGGTAACTACCAATGGAGAAATATGCCTTCTTGCAGGGGCAGCTTCAGACTGTG 4645
QUERY: 4718 ACTGCAAAAACGATGTCAATTGCAACTGCTATTCAGGAGATGATGCCTACGCGACTGATG 4777
SBJCT: 4646 ATTGCAAAAATGATGTCAACTGTAATTGCTATTCTGGGGATGATGGGTATGCCACTGATG 4705
QUERY: 4778 CCATCTTGAATTCCCCATCATCCTTAGCTGTAGCTCCAGATGGTACCATTTACATTGCAG 4837
SBJCT: 4706 CCATCTTAAATTCACCATCTTCCTTAGCTGTGGCCCCAGATGGTACCATCTACATAGCTG 4765
QUERY: 4838 ACCTTGGAAATATTCGGATCAGGGCGGTCAGCAAGAACAAGCCTGTTCTTAATGCCTTCA 4897
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QUERY: 4898 ACCAGTATGAGGCTGCATCCCCCGGAGAGCAGGAGTTATATGTTTTCAACGCTGATGGCA 4957
SBJCT: 4826 ACCAATATGAAGCTGCATCTCCAGGAGAACAGGAGCTGTATGTCTTCAATGCTGATGGGA 4885
QUERY: 4958 TCCACCAATACACTGTGAGCCTGGTGACAGGGGAGTACTTGTACAATTTCACATATAGTA 5017
SBJCT: 4886 TTCACCAGTACACTCTCAGCCTTGTTACCGGGGAGTACTTGTACAATTTCACCTATAGCA 4945
QUERY: 5018 CTGACAATGATGTCACTGAATTGATTGACAATAATGGGAATTCCCTGAAGATCCGTCGGG 5077
SBJCT: 4946 GTGATAACGATGTCACCGAGGTGATGGACAGCAATGGCAACTCCTTGAAGGTCCGTCGGG 5005
QUERY: 5078 ACAGCAGTGGCATGCCCCGTCACCTGCTCATGCCTGACAACCAGATCATCACCCTCACCG 5137
SBJCT: 5006 ATGCCAGCGGAATGCCCCGCCATTTACTGATGCCTGATAATCAGATTGTCACGCTGGCCG 5065
QUERY: 5138 TGGGCACCAATGGAGGCCTCAAAGTCGTGTCCACACAGAACCTGGAGCTTGGTCTCATGA 5197
SBJCT: 5066 TTGGCACTAATGGTGGACTCAAACTAGTCTCAACGCAGACCCTGGAACTTGGATTAATGA 5125
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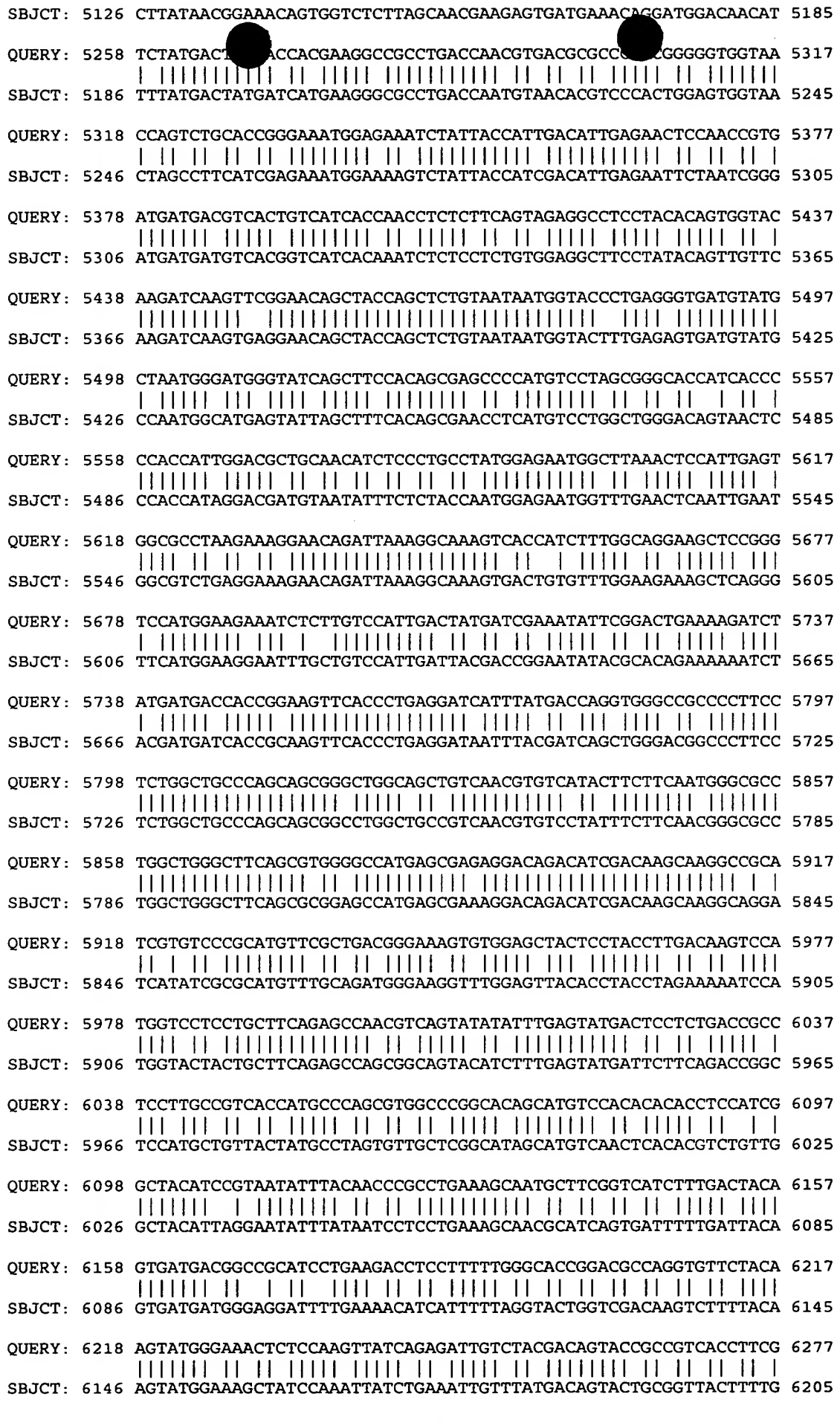
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QUERY: 5258 TCTATGACT ACCACGAAGGCCGCCTGACCAACGTGACGCGCC GGGGGTGGTAA 5317
SBJCT: 5186 TTTATGACTATGATCATGAAGGGCGCCTGACCAATGTAACACGTCCCACTGGAGTGGTAA 5245
QUERY: 5318 CCAGTCTGCACCGGGAAATGGAGAAATCTATTACCATTGACATTGAGAACTCCAACCGTG 5377
SBJCT: 5246 CTAGCCTTCATCGAGAAATGGAAAAGTCTATTACCATCGACATTGAGAATTCTAATCGGG 5305
QUERY: 5378 ATGATGACGTCACTGTCATCACCAACCTCTCTTCAGTAGAGGCCTCCTACACAGTGGTAC 5437
SBJCT: 5306 ATGATGATGTCACGGTCATCACAAATCTCTCCTCTGTGGAGGCTTCCTATACAGTTGTTC 5365
QUERY: 5438 AAGATCAAGTTCGGAACAGCTACCAGCTCTGTAATAATGGTACCCTGAGGGTGATGTATG 5497
SBJCT: 5366 AAGATCAAGTGAGGAACAGCTACCAGCTCTGTAATAATGGTACTTTGAGAGTGATGTATG 5425
QUERY: 5498 CTAATGGGATGGGTATCAGCTTCCACAGCGAGCCCCATGTCCTAGCGGGCACCATCACCC 5557
SBJCT: 5426 CCAATGGCATGAGTATTAGCTTTCACAGCGAACCTCATGTCCTGGCTGGGACAGTAACTC 5485
QUERY: 5558 CCACCATTGGACGCTGCAACATCTCCCTGCCTATGGAGAATGGCTTAAACTCCATTGAGT 5617
SBJCT: 5486 CCACCATAGGACGATGTAATATTTCTCTACCAATGGAGAATGGTTTGAACTCAATTGAAT 5545
QUERY: 5618 GGCGCCTAAGAAAGGAACAGATTAAAGGCAAAGTCACCATCTTTGGCAGGAAGCTCCGGG 5677
SBJCT: 5546 GGCGTCTGAGGAAAGAACAGATTAAAGGCAAAGTGACTGTGTTTGGAAGAAAGCTCAGGG 5605
QUERY: 5678 TCCATGGAAGAAATCTCTTGTCCATTGACTATGATCGAAATATTCGGACTGAAAAGATCT 5737
SBJCT: 5606 TTCATGGAAGGAATTTGCTGTCCATTGATTACGACCGGAATATACGCACAGAAAAAATCT 5665
QUERY: 5738 ATGATGACCACCGGAAGTTCACCCTGAGGATCATTTATGACCAGGTGGGCCGCCCCTTCC 5797
SBJCT: 5666 ACGATGATCACCGCAAGTTCACCCTGAGGATAATTTACGATCAGCTGGGACGGCCCTTCC 5725
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SBJCT: 6026 GCTACATTAGGAATATTTATAATCCTCCTGAAAGCAACGCATCAGTGATTTTTGATTACA 6085
QUERY: 6158 GTGATGACGGCCGCATCCTGAAGACCTCCTTTTTGGGCACCGGACGCCAGGTGTTCTACA 6217
SBJCT: 6086 GTGATGATGGGAGGATTTTGAAAACATCATTTTTAGGTACTGGTCGACAAGTCTTTTACA 6145
QUERY: 6218 AGTATGGGAAACTCTCCAAGTTATCAGAGATTGTCTACGACAGTACCGCCGTCACCTTCG 6277
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QUERY: 6278 GGTATGACGAGACCACTGGTGTCTTGAAGATGGTCAACCTCCAAAGTGGGGGCTTCTCCT 6337
           | |||||  ||  || ||||||  | ||  |||||  ||   | ||||  ||  ||  ||  |
SBJCT: 6206 GATATGATG  CTACAGGTGTCCTAAAAATGGTGAATTTGCAAAG  GAGGATTTTCTT 6265

QUERY: 6338 GCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTACAGGTTCTCCG 6397
           | ||  |||  |  ||  ||  ||  ||||||||  ||  ||  |||||  ||  ||||||||  |||||  |
SBJCT: 6266 GTACAATCCGCTATCGTAAAATTGGCCCTCTTGTTGACAAACAAATCTACAGATTCTCTG 6325

QUERY: 6398 AGGAAGGCATGGTCAATGCCAGGTTTGACTACACCTATCATGACAACAGCTTCCGCATCG 6457
           | ||||||  ||||||||||||  ||||||||  ||  ||  |||||  |||||  ||  ||  |||||  |
SBJCT: 6326 AAGAAGGTATGGTCAATGCAAGGTTTGATTATACATATCACGACAATAGTTTTCGCATTG 6385

QUERY: 6458 CAAGCATCAAGCCCGTCATAAGTGAGACTCCCCTCCCCGTTGACCTCTACCGCTATGATG 6517
           ||||||||||  |||  ||||||||||||||||  ||  ||  |||||  ||  |||||  |||||||
SBJCT: 6386 CAAGCATCAAACCCATCATAAGTGAGACTCCTCTTCCAGTTGATCTTTACCGTTATGATG 6445

QUERY: 6518 AGATTTCTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCATCTATTATGACATCAACC 6577
           ||||||||||||  ||  ||  ||  |||||  ||  ||||||||  ||  ||||||||  ||  ||  |
SBJCT: 6446 AGATTTCTGGCAAAGTTGAGCATTTTGGCAAATTTGGAGTTATTTATTATGATATAAATC 6505

QUERY: 6578 AGATCATCACCACTGCCGTGATGACCCTCAGCAAACACTTCGACACCCATGGGCGGATCA 6637
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SBJCT: 6506 AAATTATTACTACAGCAGTTATGACACTGAGTAAGCACTTTGATACCCACGGACGCATTA 6565

QUERY: 6638 AGGAGGTCCAGTATGAGATGTTCCGGTCCCTCATGTACTGGATGACGGTGCAATATGACA 6697
           |  ||  ||  ||  ||||||||||||||  |||||  ||||||||||||||  ||||||||||||
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QUERY: 6698 GCATGGGCAGGGTGATCAAGAGGGAGCTAAAACTGGGGCCCTATGCCAATACCACGAAGT 6757
           |||||||  ||  ||  |  ||  ||  ||  ||  |||||  |||||  ||||||||  ||  ||  ||||
SBJCT: 6626 GCATGGGAAGAGTAACTAAAAGAGAACTGAAACTTGGGCCGTATGCCAACACAACCAAGT 6685

QUERY: 6758 ACACCTATGACTACGATGGGGACGGGCAGCTCCAGAGCGTGGCCGTCAATGACCGCCCGA 6817
           |  ||||||||  ||  |||||  ||  |||||  |  ||  |||||  ||  ||  |||||  |  ||  |
SBJCT: 6686 ATACCTATGATTATGATGGAGATGGGCAATTGCAAAGCGTAGCAGTAAATGATAGGCCTA 6745

QUERY: 6818 CCTGGCGCTACAGCTATGACCTTAATGGGAATCTCCACTTACTGAACCCAGGCAACAGTG 6877
           |||||||  |||||  ||||||||  |||||  |||||  |||  |  |||||  ||  ||  |||||||
SBJCT: 6746 CCTGGCGTTACAGTTATGACCTGAATGGAAATCTTCACCTCCTGAATCCTGGAAACAGTG 6805

QUERY: 6878 TGCGCCTCATGCCCTTGCGCTATGACCTC 6906
           |  ||  |  ||||||  |||||||  ||||||
SBJCT: 6806 TTCGATTGATGCCCCTGCGCTACGACCTC 6834

 SCORE = 1241 BITS (626), EXPECT = 0.0
 IDENTITIES = 1553/1862 (83%)
 STRAND = PLUS / PLUS

QUERY: 1486 AGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCGGGTAACACAAGAAGTCCCACCA 1545
           ||||||||||  |||||  |||  ||||||||||  ||    |||  ||  |||||  ||  ||  ||
SBJCT: 1414 AGCAGCATAGATAGTGGAGAAACAGAAGTTGGCCGCAAGGTCACCCAAGAGGTGCCCCCT 1473

QUERY: 1546 GGGGTGTTTTGGAGGTCACAAATTCACATCAGTCAGCCCCAGTTCTTAAAGTTCAACATC 1605
           ||  |||||  |||  ||||  ||  ||  ||  |||||  |||||  ||||||  |  ||||||||||
SBJCT: 1474 GGAGTGTTCTGGCGGTCTCAGATCCATATCAGCCAGCCACAGTTCCTGAAGTTCAACATA 1533

QUERY: 1606 TCCCTCGGGAAGGACGCTCTCTTTGGTGTTTACATAAGAAGAGGACTTCCACCATCTCAT 1665
           |||||  ||||||||  |||||  ||  ||||||||  ||||||||||||||  ||||||||  |||
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QUERY: 1666 GCCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGAGAAGTGGAGTGTGGTTGAGTCT 1725
           ||  ||||||||  ||||||||||  ||||  |||||  |||||  ||||||||||  ||  ||
SBJCT: 1594 GCACAGTATGATTTCATGGAACGCTTGGATGGGAAAGAGAAATGGAGTGTGGTGGAATCC 1653

QUERY: 1726 CCCAGGGAACGCCGGAGCATACAGACCTTGGTTCAGAATGAAGCCGTGTTTGTGCAGTAC 1785
           ||  |||||||  ||  ||  ||  |||||  |  ||||||||||  ||  ||||||||  ||||||
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QUERY: 1786 CTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGATGGAAAAGACAAAGAGATGGTT 1845
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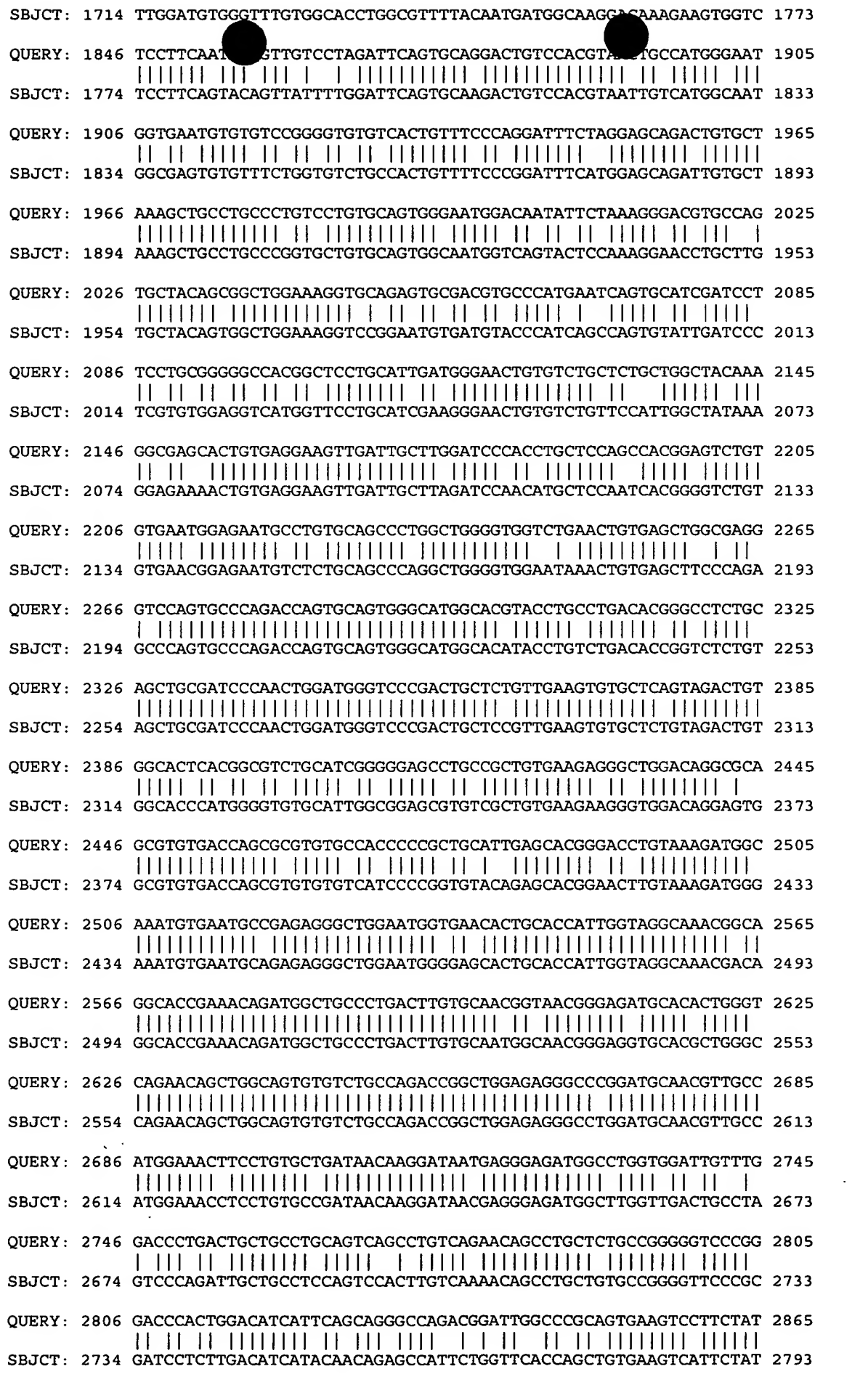
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QUERY: 1906 GGTGAATGTGTGTCCGGGGTGTGTCACTGTTTCCCAGGATTTCTAGGAGCAGACTGTGCT 1965
SBJCT: 1834 GGCGAGTGTGTTTCTGGTGTCTGCCACTGTTTTCCCGGATTTCATGGAGCAGATTGTGCT 1893
QUERY: 1966 AAAGCTGCCTGCCCTGTCCTGTGCAGTGGGAATGGACAATATTCTAAAGGGACGTGCCAG 2025
SBJCT: 1894 AAAGCTGCCTGCCCGGTGCTGTGCAGTGGCAATGGTCAGTACTCCAAAGGAACCTGCTTG 1953
QUERY: 2026 TGCTACAGCGGCTGGAAAGGTGCAGAGTGCGACGTGCCCATGAATCAGTGCATCGATCCT 2085
SBJCT: 1954 TGCTACAGTGGCTGGAAAGGTCCGGAATGTGATGTACCCATCAGCCAGTGTATTGATCCC 2013
QUERY: 2086 TCCTGCGGGGGCCACGGCTCCTGCATTGATGGGAACTGTGTCTGCTCTGCTGGCTACAAA 2145
SBJCT: 2014 TCGTGTGGAGGTCATGGTTCCTGCATCGAAGGGAACTGTGTCTGTTCCATTGGCTATAAA 2073
QUERY: 2146 GGCGAGCACTGTGAGGAAGTTGATTGCTTGGATCCCACCTGCTCCAGCCACGGAGTCTGT 2205
SBJCT: 2074 GGAGAAAACTGTGAGGAAGTTGATTGCTTAGATCCAACATGCTCCAATCACGGGGTCTGT 2133
QUERY: 2206 GTGAATGGAGAATGCCTGTGCAGCCCTGGCTGGGGTGGTCTGAACTGTGAGCTGGCGAGG 2265
SBJCT: 2134 GTGAACGGAGAATGTCTCTGCAGCCCAGGCTGGGGTGGAATAAACTGTGAGCTTCCCAGA 2193
QUERY: 2266 GTCCAGTGCCCAGACCAGTGCAGTGGGCATGGCACGTACCTGCCTGACACGGGCCTCTGC 2325
SBJCT: 2194 GCCCAGTGCCCAGACCAGTGCAGTGGGCATGGCACATACCTGTCTGACACCGGTCTCTGT 2253
QUERY: 2326 AGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCTGTTGAAGTGTGCTCAGTAGACTGT 2385
SBJCT: 2254 AGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCCGTTGAAGTGTGCTCTGTAGACTGT 2313
QUERY: 2386 GGCACTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTGTGAAGAGGGCTGGACAGGCGCA 2445
SBJCT: 2314 GGCACCCATGGGGTGTGCATTGGCGGAGCGTGTCGCTGTGAAGAAGGGTGGACAGGAGTG 2373
QUERY: 2446 GCGTGTGACCAGCGCGTGTGCCACCCCCGCTGCATTGAGCACGGGACCTGTAAAGATGGC 2505
SBJCT: 2374 GCGTGTGACCAGCGTGTGTGTCATCCCCGGTGTACAGAGCACGGAACTTGTAAAGATGGG 2433
QUERY: 2506 AAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTGCACCATTGGTAGGCAAACGGCA 2565
SBJCT: 2434 AAATGTGAATGCAGAGAGGGCTGGAATGGGGAGCACTGCACCATTGGTAGGCAAACGACA 2493
QUERY: 2566 GGCACCGAAACAGATGGCTGCCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGT 2625
SBJCT: 2494 GGCACCGAAACAGATGGCTGCCCTGACTTGTGCAATGGCAACGGGAGGTGCACGCTGGGC 2553
QUERY: 2626 CAGAACAGCTGGCAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCCGGATGCAACGTTGCC 2685
SBJCT: 2554 CAGAACAGCTGGCAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCTGGATGCAACGTTGCC 2613
QUERY: 2686 ATGGAAACTTCCTGTGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGATTGTTTG 2745
SBJCT: 2614 ATGGAAACCTCCTGTGCCGATAACAAGGATAACGAGGGAGATGGCTTGGTTGACTGCCTA 2673
QUERY: 2746 GACCCTGACTGCTGCCTGCAGTCAGCCTGTCAGAACAGCCTGCTCTGCCGGGGGTCCCGG 2805
SBJCT: 2674 GTCCCAGATTGCTGCCTCCAGTCCACTTGTCAAAACAGCCTGCTGTGCCGGGGTTCCCGC 2733
QUERY: 2806 GACCCACTGGACATCATTCAGCAGGGCCAGACGGATTGGCCCGCAGTGAAGTCCTTCTAT 2865
SBJCT: 2734 GATCCTCTTGACATCATACAACAGAGCCATTCTGGTTCACCAGCTGTGAAGTCATTCTAT 2793

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QUERY: 2866 GACCGTATCAAGCTCTTGGCAGGCAAGGATAGCACCCACATCATTCCTGGAGAGAACCCT 2925
           || || |||[redacted]||||| |  || ||||| ||||| || |||||||[redacted]|||| || ||
SBJCT: 2794 GATCGAATC[redacted]TCTTAGTGGGGAAGGACAGCACTCATATCATT[redacted]GGAGAAAATCCC 2853

QUERY: 2926 TTCAACAGCAGCTTGGTTTCTCTCATCCGAGGCCAAGTAGTAACTACAGATGGAACTCCC 2985
           |||||||||||| | || ||||| ||  |||||||||| || |||||||||||||| ||
SBJCT: 2854 TTCAACAGCAGCCTTGTGTCTCTTATAAGAGGCCAAGTGGTGACTACAGATGGAACGCCT 2913

QUERY: 2986 CTGGTCGGTGTGAACGTGTCTTTTGTCAAGTACCCAAAATACGGCTACACCATCACCCGC 3045
           || || || || |||||||| |||||||||| ||||| || ||||| |||||||| ||
SBJCT: 2914 CTAGTTGGGGTCAACGTGTCATTTGTCAAGTATCCAAAGTATGGCTATACCATCACTCGT 2973

QUERY: 3046 CAGGATGGCACGTTCGACCTGATCGCAAATGGAGGTGCTTCCTTGACTCTACACTTTGAG 3105
           |||||||||| ||| ||| || | || || || ||  | ||| | ||| | ||||||||
SBJCT: 2974 CAGGATGGCATGTTTGACTTGGTTGCTAACGGTGGATCATCCCTAACTTTGCACTTTGAA 3033

QUERY: 3106 CGAGCCCCGTTCATGAGCCAGGAGCGCACTGTGTGGCTGCCGTGGAACAGCTTTTACGCC 3165
           || ||||| || ||||| |||||  | || || ||||||||||||||||||||| || |||
SBJCT: 3034 CGGGCCCCATTTATGAGTCAGGAAAGGACAGTATGGCTGCCGTGGAACAGCTTCTATGCC 3093

QUERY: 3166 ATGGACACCCTGGTGATGAAGACCGAGGAGAACTCCATCCCCAGCTGTGACCTCAGTGGC 3225
           |||||||| || || ||||| || |||||||||||||| |||||||||| |||||||||
SBJCT: 3094 ATGGACACGCTTGTAATGAAAACAGAGGAGAACTCCATTCCCAGCTGTGATCTCAGTGGC 3153

QUERY: 3226 TTTGTCCGGCCTGATCCAATCATCATCTCCTCCCCACTGTCCACCTTCTTTAGTGCTGCC 3285
           |||||| | ||||||||| ||||||| || || |||||||| || ||||| |||| |||
SBJCT: 3154 TTTGTCAGACCTGATCCAGTCATCATTTCATCACCACTGTCAACTTTCTTCAGTGATGCT 3213

QUERY: 3286 CCTGGGCAGAATCCCATCGTGCCTGAGACCCAGGTTCTTCATGAAGAAATCGAGCTCCCT 3345
           ||||| |  ||||| || || || || ||||||||||||||||||||| ||| |||||
SBJCT: 3214 CCTGGCCGAAATCCTATTGTACCAGAAACCCAGGTTCTTCATGAAGAAATTGAGGTCCCT 3273

QUERY: 3346 GG 3347
           ||
SBJCT: 3274 GG 3275

SCORE =  547 BITS (276), EXPECT = E-152
 IDENTITIES = 540/628 (85%)
 STRAND = PLUS / PLUS

QUERY: 782  GTCGTCCCATTCCACCTACATCCTCGCCTAGTCTCCTCCCATCTGCTCAGCTGCCTAGCT 841
           |||||||||||||||||||||||||| |||| || |||||||||||||||||||| || |
SBJCT: 587  GTCGTCCCATTCCACCTACATCCTCGTCTAGCCTTCTCCCATCTGCTCAGCTGCCCAGTT 646

QUERY: 842  CCCATAATCCTCCACCAGTTAGCTGCCAGATGCCATTGCTAGACAGCAACACCTCCCATC 901
           | |||||||||||||||||||||||||||||||||||||||||||||||| || |||||||
SBJCT: 647  CTCATAATCCTCCACCAGTTAGCTGCCAGATGCCATTGCTAGACAGCAATACGTCCCATC 706

QUERY: 902  AAATCATGGACACCAACCCTGATGAGGAATTCTCCCCCAATTCATACCTGCTCAGAGCAT 961
           |||||||||||||||| ||||| ||||| ||||| || |||||||||| || |||||||
SBJCT: 707  AAATCATGGACACCAATCCTGACGAGGAGTTCTCTCCTAATTCATACCTACTAAGAGCAT 766

QUERY: 962  GCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCGAACCACCACAGCCAGTCGACTC 1021
           | |||||||| ||||| || |||||||||||||| | ||||| |||||||||| || |
SBJCT: 767  GTTCAGGGCCACAGCAGGCATCCAGCAGTGGCCCTTCAAACCATCACAGCCAGTCAACGC 826

QUERY: 1022 TGAGGCCCCCTCTCCCACCCCCTCACAACCACACGCTGTCCCATCACCACTCGTCCGCCA 1081
           ||||||| |||||||| || |||||||||||| |||||||||||| |||||||| ||||
SBJCT: 827  TGAGGCCACCTCTCCCCCCTCCTCACAACCACTCGCTGTCCCATCATCACTCGTCTGCCA 886

QUERY: 1082 ACTCCCTCAACAGGAACTCACTGACCAATCGGCGGAGTCAGATCCACGCCCCGGCCCCAG 1141
           |||||||||||||||||| || ||||| || || |  |||||||||| || || || |
SBJCT: 887  ACTCCCTCAACAGGAACTCGCTCACCAACCGCCGCAACCAGATCCACGCGCCTGCTCCCG 946

QUERY: 1142 CGCCCAATGACCTGGCCACCACACCAGAGTCCGTTCAGCTTCAGGACAGCTGGGTGCTAA 1201
           | |||||||||||||| ||||| || ||||| || ||||| |||||||||||||||| |
SBJCT: 947  CTCCCAATGACCTGGCGACCACGCCTGAGTCTGTGCAGCTGCAGGACAGCTGGGTGCTCA 1006

QUERY: 1202 ACAGCAACGTGCCACTGGAGACCCGGCACTTCCTCTTCAAGACCTCCTCGGGGAGCACAC 1261
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SBJCT: 1007 ACAGCAAC[redacted]CGCTGGAGACCAGGCATTTCTTGTTTAAGACAT[redacted]TGGAACGACTC 1066

QUERY: 1262 CCTTGTTCAGCAGCTCTTCCCCGGGATACCCTTTGACCTCAGGAACGGTTTACACGCCCC 1321
SBJCT: 1067 CGCTGTTCAGTAGCTCTTCCCCTGGCTACCCACTGACCTCAGGAACAGTTTATACTCCAC 1126

QUERY: 1322 CGCCCCGCCTGCTGCCCAGGAATACTTTCTCCAGGAAGGCTTTCAAGCTGAAGAAGCCCT 1381
SBJCT: 1127 CTCCCAGGCTGTTACCTAGAAATACATTTTCCAGGAATGCATTCAAGCTGAAAAAGCCCT 1186

QUERY: 1382 CCAAATACTGCAGCTGGAAATGTGCTGC 1409
SBJCT: 1187 CCAAGTATTGTAGCTGGAAATGTGCTGC 1214

SCORE =  391 BITS (197), EXPECT = E-105
 IDENTITIES = 593/725 (81%)
 STRAND = PLUS / PLUS

QUERY: 7156 CATGTCTACAATCACTCCAACTCGGAGATTACCTCACTGTACTACGACCTCCAGGGCCAC 7215
SBJCT: 7084 CATGTCTACAATCATTCCAATTCAGAAATTACCTCTCTGTATTATGATCTGCAAGGCCAC 7143

QUERY: 7216 CTCTTTGCCATGGAGAGCAGCAGTGGGGAGGAGTACTATGTTGCCTCTGATAACACAGGG 7275
SBJCT: 7144 CTCTTTGCAATGGAGAGTAGCAGTGGGGAAGAATATTATGTCGCCTCCGATAACACGGGC 7203

QUERY: 7276 ACTCCTCTGGCTGTGTTCAGCATCAACGGCCTCATGATCAAACAGCTGCAGTACACGGCC 7335
SBJCT: 7204 ACTCCGCTAGCCGTATTCAGCATCAATGGCCTCATGATCAAACAGCTTCAGTACACTGCA 7263

QUERY: 7336 TATGGGGAGATTTATTATGACTCCAACCCCGACTTCCAGATGGTCATTGGCTTCCATGGG 7395
SBJCT: 7264 TACGGAGAGATTTATTATGACTCAAACCCTGATTTCCAGCTGGTTATTGGGTTCCATGGA 7323

QUERY: 7396 GGACTCTATGACCCCCTGACCAAGCTGGTCCACTTCACTCAGCGTGATTATGATGTGCTG 7455
SBJCT: 7324 GGGCTGTATGATCCTTTAACCAAACTCGTCCATTTTACCCAAAGGGACTACGATGTCCTT 7383

QUERY: 7456 GCAGGACGATGGACCTCCCCAGACTATACCATGTGGAAAAACGTGGGCAAGGAGCCGGCC 7515
SBJCT: 7384 GCTGGACGCTGGACATCTCCTGATTACACAATGTGGAAAAACATTGGTAGAGAACCTGCT 7443

QUERY: 7516 CCCTTTAACCTGTATATGTTCAAGAGCAACAATCCTCTCAGCAGTGAGCTAGATTTGAAG 7575
SBJCT: 7444 CCCTTCAATCTGTACATGTTCAAGAGTAACAACCCTCTCAGCAATGAACTGGATCTAAAG 7503

QUERY: 7576 AACTACGTGACAGATGTGAAAAGCTGGCTTGTGATGTTTGGATTTCAGCTTAGCAACATC 7635
SBJCT: 7504 AATTATGTAACAGATGTCAAAAGCTGGCTGGTGATGTTCGGATTTCAGCTTAGCAACATT 7563

QUERY: 7636 ATTCCTGGCTTCCCGAGAGCCAAAATGTATTTCGTGCCTCCTCCCTATGAATTGTCAGAG 7695
SBJCT: 7564 ATTCCTGGCTTCCCTAGAGCAAAAATGTACTTTGTGTCACCTCCATACGAGCTGACTGAG 7623

QUERY: 7696 AGTCAAGCAAGTGAGAATGGACAGCTCATTACAGGTGTCCAACAGACAACAGAGAGACAT 7755
SBJCT: 7624 AGTCAAGCGTGTGAAAATGGACAGCTAATTACAGGAGTCCAGCAGACAACAGAAAGACAC 7683

QUERY: 7756 AACCAGGCCTTCATGGCTCTGGAAGGACAGGTCATTACTAAAAAGCTCCACGCCAGCATC 7815
SBJCT: 7684 AATCAAGCTTTCATGGCTCTTGAGGGACAGGTCATATCTAAAAGATTACATGCCAGTATT 7743

QUERY: 7816 CGAGAGAAAGCAGGTCACTGGTTTGCCACCACCACGCCCATCATTGGCAAAGGCATCATG 7875
SBJCT: 7744 AGAGAAAAAGCAGGCCACTGGTTTGCAACAAGCACTCCTATTATTGGGAAAGGAATCATG 7803

QUERY: 7876 TTTGC 7880
SBJCT: 7804 TTTGC 7808
```

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SCORE =  339 BITS (17[redacted] EXPECT = 2E-89
 IDENTITIES = 429/515 [redacted]%)
 STRAND = PLUS / PLUS

QUERY: 7967 ACTACCTGGACAAGATGCACTACAGCATCGAGGGCAAGGACACCCACTACTTTGTGAAGA 8026
           |||||||||| || ||||||||||||||||||| ||||| || |||||||||||| ||||
SBJCT: 7895 ACTACCTGGAAAAAATGCACTACAGCATCGAGGGGAAGGATACTCACTACTTTGTCAAGA 7954

QUERY: 8027 TTGGCTCAGCCGATGGCGACCTGGTCACACTAGGCACCACCATCGGCCGCAAGGTGCTAG 8086
           | |||||||||||| ||||||| ||||| || |  |  |||| |||  | ||||| || |
SBJCT: 7955 TAGGCTCAGCCGATAGCGACCTCGTCACCCTCGCGATGACCAGCGGGAGGAAGGTCCTGG 8014

QUERY: 8087 AGAGCGGGGTGAACGTGACCGTGTCCCAGCCCACGCTGCTGGTCAACGGCAGGACTCGAA 8146
           | ||||| || |||||||||| |||||||| || || ||  ||||||| |||||||||
SBJCT: 8015 ACAGCGGAGTAAACGTGACCGTCTCCCAGCCAACCCTCCTTATCAACGGAAGGACTCGAC 8074

QUERY: 8147 GGTTCACGAACATTGAGTTCCAGTACTCCACGCTGCTGCTCAGCATCCGCTATGGCCTCA 8206
           ||||||| ||||| ||||| ||||| ||||| |||||| ||| |||||||| || ||||
SBJCT: 8075 GGTTCACAAACATCGAGTTTCAGTATTCCACCCTGCTGATCAACATCCGCTACGGGCTCA 8134

QUERY: 8207 CCCCCGACACCCTGGACGAAGAGAAGGCCCGCGTCCTGGACCAGGCGAGACAGAGGGCCC 8266
           || ||||||| ||||| || |||||||| || || || ||||||||  | ||| | ||||
SBJCT: 8135 CCGCCGACACGCTGGATGAGGAGAAGGCACGAGTGCTAGACCAGGCTCGGCAGCGAGCCC 8194

QUERY: 8267 TGGGCACGGCCTGGGCCAAGGAGCAGCAGAAAGCCAGGGACGGGAGAGAGGGGAGCCGCC 8326
           ||||  |||||||||||| |||||||||| ||  |||| ||  | ||||| ||||||
SBJCT: 8195 TGGGGTCGGCCTGGGCCAAAGAGCAGCAGAAGGCACGGGATGGCCGCGAGGGCAGCCGCG 8254

QUERY: 8327 TGTGGACTGAGGGCGAGAAGCAGCAGCTTCTGAGCACCGGGCGCGTGCAAGGGTACGAGG 8386
           | ||||| || || |||||||| |||||||||| ||| ||  | || ||||| |||||||
SBJCT: 8255 TATGGACAGACGGAGAGAAGCAACAGCTTCTGAACACGGGAAGGGTTCAAGGTTACGAGG 8314

QUERY: 8387 GATATTACGTGCTTCCCGTGGAGCAATACCCAGAGCTTGCAGACAGTAGCAGCAACATCC 8446
           ||||||| ||  | || |||||||| |||||||||| ||||||||||||||||||||||
SBJCT: 8315 GATATTATGTCTTGCCTGTGGAGCAGTACCCAGAGCTAGCAGACAGTAGCAGCAACATCC 8374

QUERY: 8447 AGTTTTTAAGACAGAATGAGATGGGAAAGAGGTAA 8481
           |||||||||||||||||| ||||||||||||||||
SBJCT: 8375 AGTTTTTAAGACAGAATGAAATGGGAAAGAGGTAA 8409

 SCORE =  323 BITS (163), EXPECT = 1E-84
 IDENTITIES = 397/475 (83%)
 STRAND = PLUS / PLUS

QUERY: 299 GACACCGCTCTTTGACCAGAGGACGCTGTGGCAAAGAGTGTCGCTACACAAGCTCCTCTC 358
           |||||||||||||||| ||||| || || || || |||||||||| || || || || |
SBJCT: 20  GACACCGCTCTTTGACGAGAGGCCGGTGCGGGAAGGAGTGTCGCTATACTAGTTCTTCAC 79

QUERY: 359 TGGACAGTGAGGACTGCCGGGTGCCCACACAGAAATCCTACAGCTCCAGTGAGACTCTGA 418
           | |||||||| |||||| | || ||  | ||||| ||||||||||||||||||||| ||||
SBJCT: 80  TCGACAGTGAAGACTGCAGAGTACCAGCTCAGAAGTCCTACAGCTCCAGTGAGACCCTGA 139

QUERY: 419 AGGCCTATGACCATGACAGCAGGATGCACTATGGAAACCGAGTCACAGACCTCATCCACC 478
           | || |||| |||||||| |||||||||| ||||| |||||  ||||||| | |||
SBJCT: 140 AAGCATATGGCCATGACACGAGGATGCACTACGGAAATCGAGTTTCAGACCTGGTTCACA 199

QUERY: 479 GGGAGTCAGATGAGTTTCCTAGACAAGGAACCAACTTCACCCTTGCCGAACTGGGCATCT 538
           ||||||| |||||||||| || |||||||| |||||||||||||| |||||||| ||||
SBJCT: 200 GGGAGTCGGATGAGTTTCCAAGGCAAGGAACGAACTTCACCCTTGCAGAACTGGGAATCT 259

QUERY: 539 GTGAGCCCTCCCCACACCGAAGCGGCTACTGCTCCGACATGGGGATCCTTCACCAGGGCT 598
           |||||||||| || || ||||| |||||||||| ||||| || || || || || ||||
SBJCT: 260 GTGAGCCCTCTCCCCATCGAAGTGGCTACTGCTCGGACATAGGAATACTCCATCAAGGCT 319

QUERY: 599 ACTCCCTTAGCACAGGGTCTGACGCCGACTCCGACACCGAGGGAGGGATGTCTCCAGAAC 658
           | ||| | ||||| || ||||| || ||||| ||||| ||||| |||||||||||||| |
SBJCT: 320 ATTCCTTGAGCACTGGCTCTGATGCTGACTCAGACACGGAGGGCGGGATGTCTCCAGAGC 379

QUERY: 659 ACGCCATCAGACTGTGGGGCAGAGGGATAAAATCCAGGCGCAGTTCCGGCCTGTCCAGTC 718
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SBJCT: 380 ACGCGATCAC[redacted]GTGGGGAAGAGGGATCAAATCCAGCCGAAGTTC[redacted]CTGTCAAGTC 439

QUERY: 719 GTGAAAACTCGGCCCTTACCCTGACTGACTCTGACAACGAAAACAAATCAGATGA 773
SBJCT: 440 GTGAAAACTCGGCTCTCACGCTCACTGACTCCGACAATGAGAACAAGTCAGATGA 494
```

The full FCTR3a amino acid sequence also has 342 of 383 amino acid residues (89%) identical to, and 342 of 383 residues (89%) positive with, the 276 amino acid residue Odd Oz/ten-m homolog 2 (*Drosophila*) (GenBank Acc: NP_035986.2) (SEQ ID NO:68) (Table 3P).

Table 3P. BLASTP of FCTR3a against Odd Oz/ten-m homolog 2 - (SEQ ID NO:68)

```
>GI|7657415|REF|NP_035986.2| ODD OZ/TEN-M HOMOLOG 2 (DROSOPHILA); ODD OZ/TEN-M HOMOLOG
3
          (DROSOPHILA) [MUS MUSCULUS]
 GI|4760778|DBJ|BAA77397.1| (AB025411) TEN-M2 [MUS MUSCULUS]
          LENGTH = 2764

 SCORE =  495 BITS (1274), EXPECT = E-139
 IDENTITIES = 342/383 (89%), POSITIVES = 342/383 (89%), GAPS = 41/383 (10%)

QUERY: 37  HNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTL 96
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 189 HNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTL 248

QUERY: 97  RPPLPPPHNHTLSHHHSSANSLNRNSLTNRRSQIHAPAPAPNDLATTPESVQLQDSWVLN 156
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 249 RPPLPPPHNHTLSHHHSSANSLNRNSLTNRRSQIHAPAPAPNDLATTPESVQLQDSWVLN 308

QUERY: 157 SNVPLETRHFLFKTSSGSTPLFSSSSPGYPLTSGTVYTPPPRLLPRNTFSRKAFKLKKPS 216
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 309 SNVPLETRHFLFKTSSGSTPLFSSSSPGYPLTSGTVYTPPPRLLPRNTFSRKAFKLKKPS 368

QUERY: 217 KYCSWKCAALSAIAAALLLAILLAYFI-------------------------------- 243
          ||||||||||||||||||||||||||
SBJCT: 369 KYCSWKCAALSAIAAALLLAILLAYFIAMHLLGLNWQLQPADGHTFNNGVRTGLPGNDDV 428

QUERY: 244 --------VPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQIHISQPQFLKFNISLGKD 295
                  ||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 429 ATVPSGGKVPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQIHISQPQFLKFNISLGKD 488

QUERY: 296 ALFGVYIRRGLPPSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVFVQYLDVGL 355
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 489 ALFGVYIRRGLPPSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVFVQYLDVGL 548

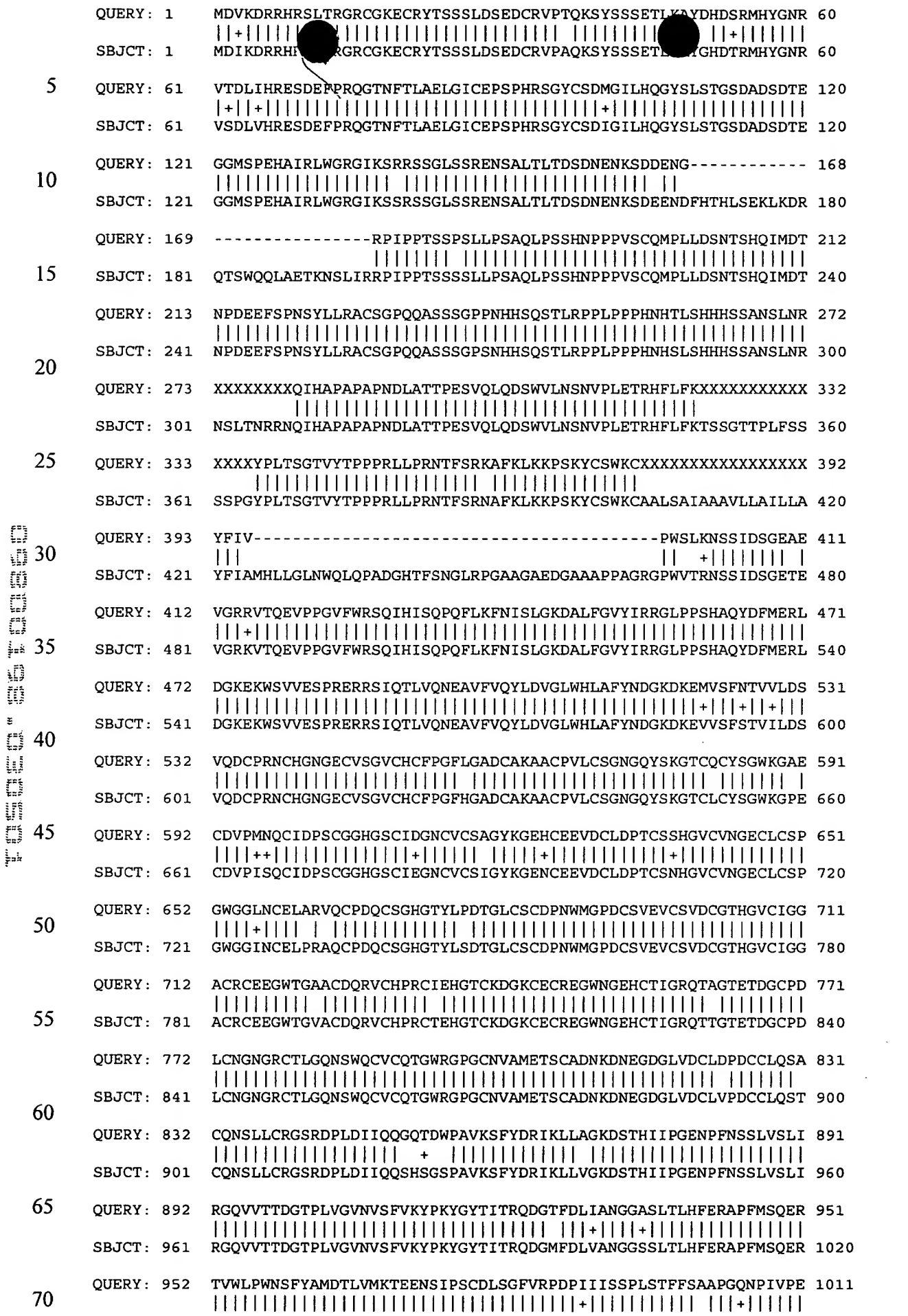
QUERY: 356 WHLAFYNDGKDKEMVSFNTVVLD 378
          |||||||||||||||||||||||
SBJCT: 549 WHLAFYNDGKDKEMVSFNTVVLD 571
```

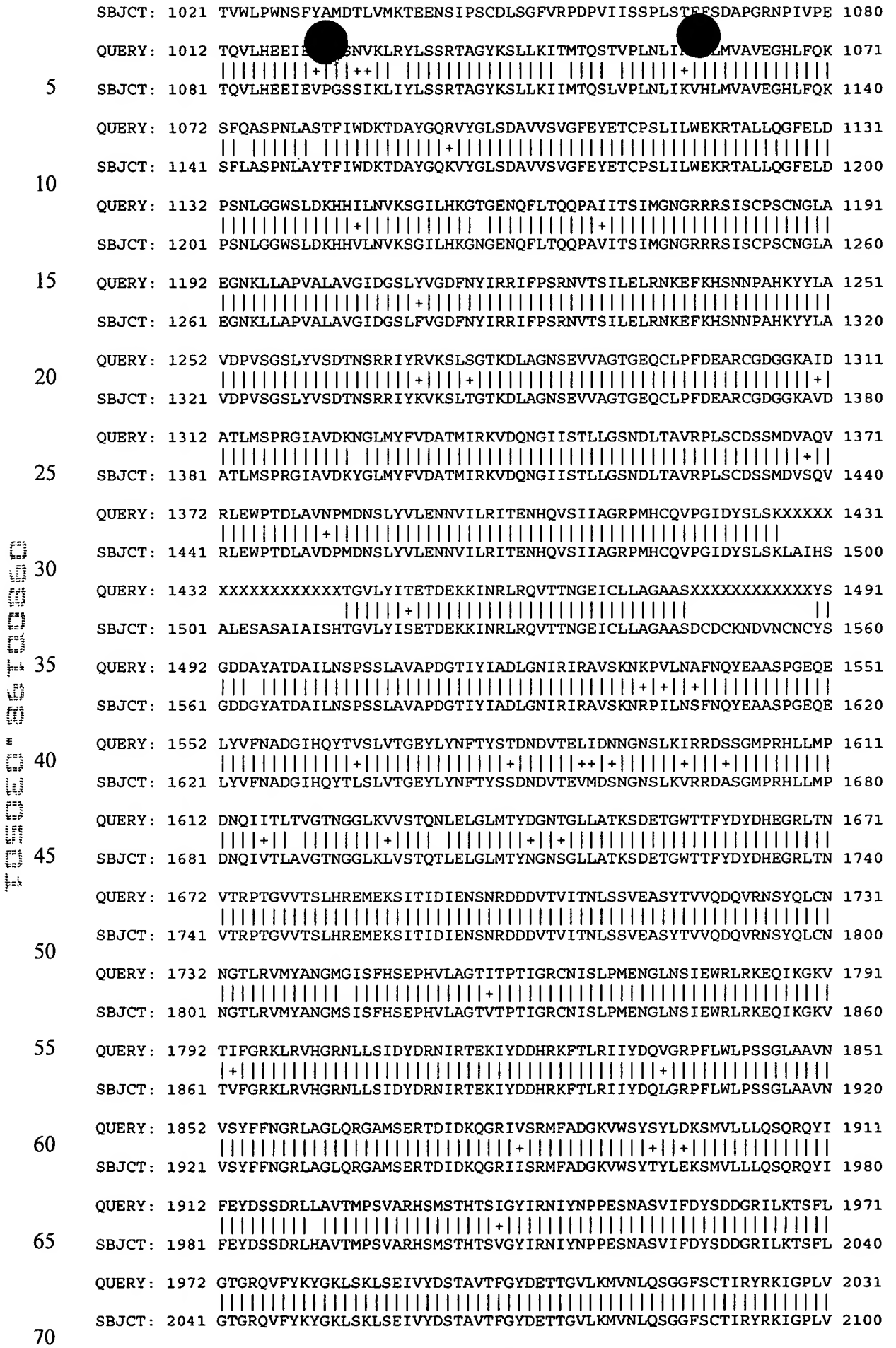
The full FCTR3b amino acid sequence has 2442 of 2802 amino acid residues (87%) identical to, and 2532 of 2802 residues (90%) positive with, the 2802 amino acid residue teneurin-2 [*Gallus gallus*] (GenBank Acc: AJ279031) (SEQ ID NO:69) (Table 3Q).

Table 3Q. BLASTP of FCTR3a against Teneurin-2 - (SEQ ID NO:69

```
>GI|10241574|EMB|CAC09416.1| (AJ279031) TENEURIN-2 [GALLUS GALLUS]
          LENGTH = 2802

 SCORE = 4853 BITS (12589), EXPECT = 0.0
 IDENTITIES = 2510/2802 (87%), POSITIVES = 2600/2802 (90%), GAPS = 69/2802 (2%)
```


QUERY: 1 MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNR 60
SBJCT: 1 MDIKDRRH RGRCGKECRYTSSSLDSEDCRVPAQKSYSSSETL GHDTRMHYGNR 60
QUERY: 61 VTDLIHRESDEFPRQGTNFTLAELGICEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTE 120
SBJCT: 61 VSDLVHRESDEFPRQGTNFTLAELGICEPSPHRSGYCSDIGILHQGYSLSTGSDADSDTE 120
QUERY: 121 GGMSPEHAIRLWGRGIKSRRSSGLSSRENSALTLTDSDNENKSDDENG---------- 168
SBJCT: 121 GGMSPEHAIRLWGRGIKSSRSSGLSSRENSALTLTDSDNENKSDEENDFHTHLSEKLKDR 180
QUERY: 169 ----------RPIPPTSSPSLLPSAQLPSSHNPPPVSCQMPLLDSNTSHQIMDT 212
SBJCT: 181 QTSWQQLAETKNSLIRRPIPPTSSSSLLPSAQLPSSHNPPPVSCQMPLLDSNTSHQIMDT 240
QUERY: 213 NPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTLRPPLPPPHNHTLSHHHSSANSLNR 272
SBJCT: 241 NPDEEFSPNSYLLRACSGPQQASSSGPSNHHSQSTLRPPLPPPHNHSLSHHHSSANSLNR 300
QUERY: 273 XXXXXXXXQIHAPAPAPNDLATTPESVQLQDSWVLNSNVPLETRHFLFKXXXXXXXXXXX 332
SBJCT: 301 NSLTNRRNQIHAPAPAPNDLATTPESVQLQDSWVLNSNVPLETRHFLFKTSSGTTPLFSS 360
QUERY: 333 XXXXYPLTSGTVYTPPPRLLPRNTFSRKAFKLKKPSKYCSWKCXXXXXXXXXXXXXXXXX 392
SBJCT: 361 SSPGYPLTSGTVYTPPPRLLPRNTFSRNAFKLKKPSKYCSWKCAALSAIAAAVLLAILLA 420
QUERY: 393 YFIV----------PWSLKNSSIDSGEAE 411
SBJCT: 421 YFIAMHLLGLNWQLQPADGHTFSNGLRPGAAGAEDGAAAPPAGRGPWVTRNSSIDSGETE 480
QUERY: 412 VGRRVTQEVPPGVFWRSQIHISQPQFLKFNISLGKDALFGVYIRRGLPPSHAQYDFMERL 471
SBJCT: 481 VGRKVTQEVPPGVFWRSQIHISQPQFLKFNISLGKDALFGVYIRRGLPPSHAQYDFMERL 540
QUERY: 472 DGKEKWSVVESPRERRSIQTLVQNEAVFVQYLDVGLWHLAFYNDGKDKEMVSFNTVVLDS 531
SBJCT: 541 DGKEKWSVVESPRERRSIQTLVQNEAVFVQYLDVGLWHLAFYNDGKDKEVVSFSTVILDS 600
QUERY: 532 VQDCPRNCHGNGECVSGVCHCFPGFLGADCAKAACPVLCSGNGQYSKGTCQCYSGWKGAE 591
SBJCT: 601 VQDCPRNCHGNGECVSGVCHCFPGFHGADCAKAACPVLCSGNGQYSKGTCLCYSGWKGPE 660
QUERY: 592 CDVPMNQCIDPSCGGHGSCIDGNCVCSAGYKGEHCEEVDCLDPTCSSHGVCVNGECLCSP 651
SBJCT: 661 CDVPISQCIDPSCGGHGSCIEGNCVCSIGYKGENCEEVDCLDPTCSNHGVCVNGECLCSP 720
QUERY: 652 GWGGLNCELARVQCPDQCSGHGTYLPDTGLCSCDPNWMGPDCSVEVCSVDCGTHGVCIGG 711
SBJCT: 721 GWGGINCELPRAQCPDQCSGHGTYLSDTGLCSCDPNWMGPDCSVEVCSVDCGTHGVCIGG 780
QUERY: 712 ACRCEEGWTGAACDQRVCHPRCIEHGTCKDGKCECREGWNGEHCTIGRQTAGTETDGCPD 771
SBJCT: 781 ACRCEEGWTGVACDQRVCHPRCTEHGTCKDGKCECREGWNGEHCTIGRQTTGTETDGCPD 840
QUERY: 772 LCNGNGRCTLGQNSWQCVCQTGWRGPGCNVAMETSCADNKDNEGDGLVDCLDPDCCLQSA 831
SBJCT: 841 LCNGNGRCTLGQNSWQCVCQTGWRGPGCNVAMETSCADNKDNEGDGLVDCLVPDCCLQST 900
QUERY: 832 CQNSLLCRGSRDPLDIIQQGQTDWPAVKSFYDRIKLLAGKDSTHIIPGENPFNSSLVSLI 891
SBJCT: 901 CQNSLLCRGSRDPLDIIQQSHSGSPAVKSFYDRIKLLVGKDSTHIIPGENPFNSSLVSLI 960
QUERY: 892 RGQVVTTDGTPLVGVNVSFVKYPKYGYTITRQDGTFDLIANGGASLTLHFERAPFMSQER 951
SBJCT: 961 RGQVVTTDGTPLVGVNVSFVKYPKYGYTITRQDGMFDLVANGGSSLTLHFERAPFMSQER 1020
QUERY: 952 TVWLPWNSFYAMDTLVMKTEENSIPSCDLSGFVRPDPIIISSPLSTFFSAAPGQNPIVPE 1011


SBJCT: 1021 TVWLPWNSFYAMDTLVMKTEENSIPSCDLSGFVRPDPVIISSPLSTFFSDAPGRNPIVPE 1080
QUERY: 1012 TQVLHEEIE SNVKLRYLSSRTAGYKSLLKITMTQSTVPLNLI MVAVEGHLFQK 1071
SBJCT: 1081 TQVLHEEIEVPGSSIKLIYLSSRTAGYKSLLKIIMTQSLVPLNLIKVHLMVAVEGHLFQK 1140
QUERY: 1072 SFQASPNLASTFIWDKTDAYGQRVYGLSDAVVSVGFEYETCPSLILWEKRTALLQGFELD 1131
SBJCT: 1141 SFLASPNLAYTFIWDKTDAYGQKVYGLSDAVVSVGFEYETCPSLILWEKRTALLQGFELD 1200
QUERY: 1132 PSNLGGWSLDKHHILNVKSGILHKGTGENQFLTQQPAIITSIMGNGRRRSISCPSCNGLA 1191
SBJCT: 1201 PSNLGGWSLDKHHVLNVKSGILHKGNGENQFLTQQPAVITSIMGNGRRRSISCPSCNGLA 1260
QUERY: 1192 EGNKLLAPVALAVGIDGSLYVGDFNYIRRIFPSRNVTSILELRNKEFKHSNNPAHKYYLA 1251
SBJCT: 1261 EGNKLLAPVALAVGIDGSLFVGDFNYIRRIFPSRNVTSILELRNKEFKHSNNPAHKYYLA 1320
QUERY: 1252 VDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGEQCLPFDEARCGDGGKAID 1311
SBJCT: 1321 VDPVSGSLYVSDTNSRRIYKVKSLTGTKDLAGNSEVVAGTGEQCLPFDEARCGDGGKAVD 1380
QUERY: 1312 ATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTAVRPLSCDSSMDVAQV 1371
SBJCT: 1381 ATLMSPRGIAVDKYGLMYFVDATMIRKVDQNGIISTLLGSNDLTAVRPLSCDSSMDVSQV 1440
QUERY: 1372 RLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSIIAGRPMHCQVPGIDYSLSKXXXXX 1431
SBJCT: 1441 RLEWPTDLAVDPMDNSLYVLENNVILRITENHQVSIIAGRPMHCQVPGIDYSLSKLAIHS 1500
QUERY: 1432 XXXXXXXXXXXXTGVLYITETDEKKINRLRQVTTNGEICLLAGAASXXXXXXXXXXXXYS 1491
SBJCT: 1501 ALESASAIAISHTGVLYISETDEKKINRLRQVTTNGEICLLAGAASDCDCKNDVNCNCYS 1560
QUERY: 1492 GDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVLNAFNQYEAASPGEQE 1551
SBJCT: 1561 GDDGYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNRPILNSFNQYEAASPGEQE 1620
QUERY: 1552 LYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELIDNNGNSLKIRRDSSGMPRHLLMP 1611
SBJCT: 1621 LYVFNADGIHQYTLSLVTGEYLYNFTYSSDNDVTEVMDSNGNSLKVRRDASGMPRHLLMP 1680
QUERY: 1612 DNQIITLTVGTNGGLKVVSTQNLELGLMTYDGNTGLLATKSDETGWTTFYDYDHEGRLTN 1671
SBJCT: 1681 DNQIVTLAVGTNGGLKLVSTQTLELGLMTYNGNSGLLATKSDETGWTTFYDYDHEGRLTN 1740
QUERY: 1672 VTRPTGVVTSLHREMEKSITIDIENSNRDDDVTVITNLSSVEASYTVVQDQVRNSYQLCN 1731
SBJCT: 1741 VTRPTGVVTSLHREMEKSITIDIENSNRDDDVTVITNLSSVEASYTVVQDQVRNSYQLCN 1800
QUERY: 1732 NGTLRVMYANGMGISFHSEPHVLAGTITPTIGRCNISLPMENGLNSIEWRLRKEQIKGKV 1791
SBJCT: 1801 NGTLRVMYANGMSISFHSEPHVLAGTVTPTIGRCNISLPMENGLNSIEWRLRKEQIKGKV 1860
QUERY: 1792 TIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLRIIYDQVGRPFLWLPSSGLAAVN 1851
SBJCT: 1861 TVFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLRIIYDQLGRPFLWLPSSGLAAVN 1920
QUERY: 1852 VSYFFNGRLAGLQRGAMSERTDIDKQGRIVSRMFADGKVWSYSYLDKSMVLLLQSQRQYI 1911
SBJCT: 1921 VSYFFNGRLAGLQRGAMSERTDIDKQGRIISRMFADGKVWSYTYLEKSMVLLLQSQRQYI 1980
QUERY: 1912 FEYDSSDRLLAVTMPSVARHSMSTHTSIGYIRNIYNPPESNASVIFDYSDDGRILKTSFL 1971
SBJCT: 1981 FEYDSSDRLHAVTMPSVARHSMSTHTSVGYIRNIYNPPESNASVIFDYSDDGRILKTSFL 2040
QUERY: 1972 GTGRQVFYKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMVNLQSGGFSCTIRYRKIGPLV 2031
SBJCT: 2041 GTGRQVFYKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMVNLQSGGFSCTIRYRKIGPLV 2100

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QUERY: 2032 DKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLPVDLYRIDEISGKVEHFGKF 2091
SBJCT: 2101 DKQIYRFS[redacted]VNARFDYTYHDNSFRIASIKPIISETPLPVDLY[redacted]EISGKVEHFGKF 2160

QUERY: 2092 GVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTVQYDSMGRVIKRELKL 2151
SBJCT: 2161 GVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTVQYDSMGRVTKRELKL 2220

QUERY: 2152 GPYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDXXXXXXXXXXXXSVRLMPLRYDLRD 2211
SBJCT: 2221 GPYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDLNGNLHLLNPGNSVRLMPLRYDLRD 2280

QUERY: 2212 RITRLGDVQYKIDDDGYLCQRGSDIFEYNSKGLLTRAYNKASGWSVQYRYDGVGRRASYK 2271
SBJCT: 2281 RITRLGDIPYKIDDDGFLCQRGSDVFEYNSKGLLTRAYNKANGWNVQYRYDGLGRRASCK 2340

QUERY: 2272 TNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGHLFAMESSSGEEYYVASDNT 2331
SBJCT: 2341 TNLGHHLQYFYADLHNPTRVTHVYNHSNSEITSLYYDLQGHLFAMESSSGEEYYVASDNT 2400

QUERY: 2332 GTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHGGLYDPLTKLVHFTQRDYDV 2391
SBJCT: 2401 GTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQLVIGFHGGLYDPLTKLVHFTQRDYDV 2460

QUERY: 2392 LAGRWTSPDYTMWKNVGKEPAPFNLYMFKSNNPLSSELDLKNYVTDVKSWLVMFGFQLSN 2451
SBJCT: 2461 LAGRWTSPDYTMWKNIGREPAPFNLYMFKSNNPLSNELDLKNYVTDVKSWLVMFGFQLSN 2520

QUERY: 2452 IIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQAFMALEGQVITKKLHAS 2511
SBJCT: 2521 IIPGFPRAKMYFVSPPYELTESQACENGQLITGVQQTTERHNQAFMALEGQVISKRLHAS 2580

QUERY: 2512 IREKAGHWFATTTPIIGKGIMFAIKEGRVTTGVSSIASEDSRKVASVLNNAYYLDKMHYS 2571
SBJCT: 2581 IREKAGHWFATSTPIIGKGIMFAVKKGRVTTGISSIATDDSRKIASVLNSAHYLEKMHYS 2640

QUERY: 2572 IEGKDTHYFVKIGSADGDLVTLGTTIGRKVLESGVNVTVSQPTLLVNGRTRRFTNIEFQY 2631
SBJCT: 2641 IEGKDTHYFVKIGSADSDLVTLAMTSGRKVLDSGVNVTVSQPTLLINGRTRRFTNIEFQY 2700

QUERY: 2632 STLLLSIRYGLTPDTLDEEKARVLDQARQRALGTAWAKEQQKARDGREGSRLWTEGEKQQ 2691
SBJCT: 2701 STLLINIRYGLTADTLDEEKARVLDQARQRALGSAWAKEQQKARDGREGSRVWTDGEKQQ 2760

QUERY: 2692 LLSTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNEMGKR 2733
SBJCT: 2761 LLNTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNEMGKR 2802
```

The FCTR3bcde and f amino acid sequences have 1524 of 2352 amino acid residues (64%) identical to, and 1881 of 2532 residues (79%) positive with, the amino acid residues 429-2771, 93 of 157 residues (59%) identical to and 118 of 157 residues (74%) positive with amino acid residues 1-155, and 59 of 152 residues (38%) identical to and 68 of 152 residues (43%) positive with amino acid residues 211-361 of Ten-m4 [*Mus musculus*] (ptnr: GenBank Acc: BAA77399.1) (SEQ ID NO:70) (Table 3R).

Table 3R. BLASTP of FCTR3b, c, d, e, and f against *Mus musculus* Ten-m4 - (SEQ ID NO:70)

```
>GI|4760782|DBJ|BAA77399.1| (AB025413) TEN-M4 [MUS MUSCULUS]
          LENGTH = 2771

 SCORE = 3089 BITS (8008), EXPECT = 0.0
```

IDENTITIES = 1524/2352 (64%), POSITIVES = 1881/2352 (79%), GAPS = 28/2352 (1%)

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QUERY: 401  KNSSIDSGE GRRVTQEVPPGVFWRSQIHISQPQFLKFNISLGK LFGVYIRRGLPP 460
            ++| ||||| +|||| +|++||| |||||+ |  |  ||||+|||| || |+| |+||||
SBJCT: 429  EDSFIDSGEIDVGRRASQKIPPGTFWRSQVFIDHPVHLKFNVSLGKAALVGIYGRKGLPP 488

QUERY: 461  SHAQYDFMERLDGK-----EKWSVVESPRERRSIQTLVQNEAVFVQYLDVGLWHLAFYND 515
            || |+||+| |||+     |  |+    |+ |       +|  |+|||| |+||||||||
SBJCT: 489  SHTQFDFVELLDGRRLLTQEARSLEGPQRQSRGPVPPSSHETGFIQYLDSGIWHLAFYND 548

QUERY: 516  GKDKEMVSFNTVVLDSVQDCPRNCHGNGECVSGVCHCFPGFLGADCAKAACPVLCSGNGQ 575
            ||+ |+||| |  ++|| +|| ||+|||+|+|| |||| |||| || +|+||||||||||
SBJCT: 549  GKESEVVSFLTTAIESVDNCPSNCYGNGDCISGTCHCFLGFLGPDCGRASCPVLCSGNGQ 608

QUERY: 576  YSKGTCQCYSGWKGAECDVPMNQCIDPSCGGHGSCIDGNCVCSAGYKGEHCEEVDCLDPT 635
            | || | |+|||||||||| ||||| +|  ||+|| | |+|+ ||||| ||||||+|||
SBJCT: 609  YMKGRCLCHSGWKGAECDVPTNQCIDVACSSHGTCIMGTCICNPGYKGESCEEVDCMDPT 668

QUERY: 636  CSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDTGLCSCDPNWMGPDCSV 695
            ||| |||| ||| || |||| |||  |  | ||||||||+|||||||+|||+| | |||+
SBJCT: 669  CSSRGVCVRGECHCSVGWGGTNCETPRATCLDQCSGHGTFLPDTGLCNCDPSWTGHDCSI 728

QUERY: 696  EVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTCKDGKCECREGWNGEHC 755
            |+|+ ||| ||||+|| ||||+|| ||||||| ||||| |||||+|||||  |||||||
SBJCT: 729  EICAADCGGHGVCVGGTCRCEDGWMGAACDQRACHPRCAEHGTCRDGKCECSPGWNGEHC 788
              *********
QUERY: 756  TIGRQTAGTETDGCPDLCNGNGRCTLGQNSWQCVCQTGWRGPGCNVAMETSCADNKDNEG 815
            ||          +||| |||||||||  | | |||| |||| ||+ +||| | | |||+|
SBJCT: 789  TIAHYLDRVVKEGCPGLCNGNGRCTLDLNGWHCVCQLGWRGTGCDTSMETGCGDGKDNDG 848

QUERY: 816  DGLVDCLDPDCCLQSACQNSLLCRGSRDPLDIIQQGQT--DWPAVKSFYDRIKLLAGKDS 873
            ||||||+|||||||  |  + || || |||||||+ |       +  |||||| | |+||
SBJCT: 849  DGLVDCMDPDCCLQPLCHVNPLCLGSPDPLDIIQETQAPVSQQNLNPFYDRIKFLVGRDS 908

QUERY: 874  THIIPGENPFNSSLVSLIRGQVVTTDGTPLVGVNVSFVKYPKYGYTITRQDGTFDLIANG 933
            || |||||||+     +|||||+|+|||||||||+||+  | +||||+||||+|||+ ||
SBJCT: 909  THSIPGENPFDGGHACVIRGQVMTSDGTPLVGVNISFINNPLFGYTISRQDGSFDLVTNG 968

QUERY: 934  GASLTLHFERAPFMSQERTVWLPWNSFYAMDTLVMKTEENSIPSCDLSGFVRPDPIIISS 993
            | |+ | ||||||++|| |+||||+ |+ |+|+||+ ||| ||||||| | ||+|++  |
SBJCT: 969  GISIILRFERAPFITQEHTLWLPWDRFFVMETIVMRHEENEIPSCDLSNFARPNPVVSPS 1028

QUERY: 994  PLSTFFSAAPGQNPIVPETQVLHEEIELPGSNVKLRYLSSRTAGYKSLLKITMTQSTVPL 1053
            ||++| |+   + ||||| | | ||| + |  ++| |||||| ||||+|+|++|  |+|
SBJCT: 1029 PLTSFASSCAEKGPIVPEIQALQEEIVIAGCKMRLSYLSSRTPGYKSVLRISLTHPTIPF 1088

QUERY: 1054 NLIRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLSDAVVSVGFEYETCP 1113
            ||++|||||||| ||+| | |+|+|+  ||||||| | |+|+| |+| ||||+|||+||
SBJCT: 1089 NLMKVHLMVAVEGRLFRKWFAAAPDLSYYFIWDKTDVYNQKVFGFSEAFVSVGYEYESCP 1148

QUERY: 1114 SLILWEKRTALLQGFELDPSNLGGWSLDKHHILNVKSGILHKGTGENQFLTQQPAIITSI 1173
            |||||||||+|||+|+| | |||||||||| ||++|||||| |||||++||| +| ||
SBJCT: 1149 DLILWEKRTAVLQGYEIDASKLGGWSLDKHHALNIQSGILHKGNGENQFVSQQPPVIGSI 1208

QUERY: 1174 MGNGRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIRRIFPSRNVTSILEL 1233
            |||||||||||||||||+|||||||||| | |||||||||||||||| |||+|||+
SBJCT: 1209 MGNGRRRSISCPSCNGLADGNKLLAPVALTCGSDGSLYVGDFNYIRRIFPSGNVTNILEM 1268

QUERY: 1234 RNKEFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGE 1293
            |||+|+||++|||||||| ||+||++++|||||+++||| +  |||  |||||||||+
SBJCT: 1269 RNKDFRHSHSPAHKYYLATDPMSGAVFLSDTNSRRVFKVKSTTVVKDLVKNSEVVAGTGD 1328

QUERY: 1294 QCLPFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSND 1353
            ||||||+ |||||||| +||| +|||| ||| ||+|||| ||||+|||||||||||||||
SBJCT: 1329 QCLPFDDTRCGDGGKATEATLTNPRGITVDKFGLIYFVDGTMIRRVDQNGIISTLLGSND 1388

QUERY: 1354 LTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSIIAGRPM 1413
            ||+ ||||||| |+++|||||||||+||||||||||+|||+|+|+||||| |+|||||
SBJCT: 1389 LTSARPLSCDSVMEISQVRLEWPTDLAINPMDNSLYVLDNNVVLQISENHQVRIVAGRPM 1448
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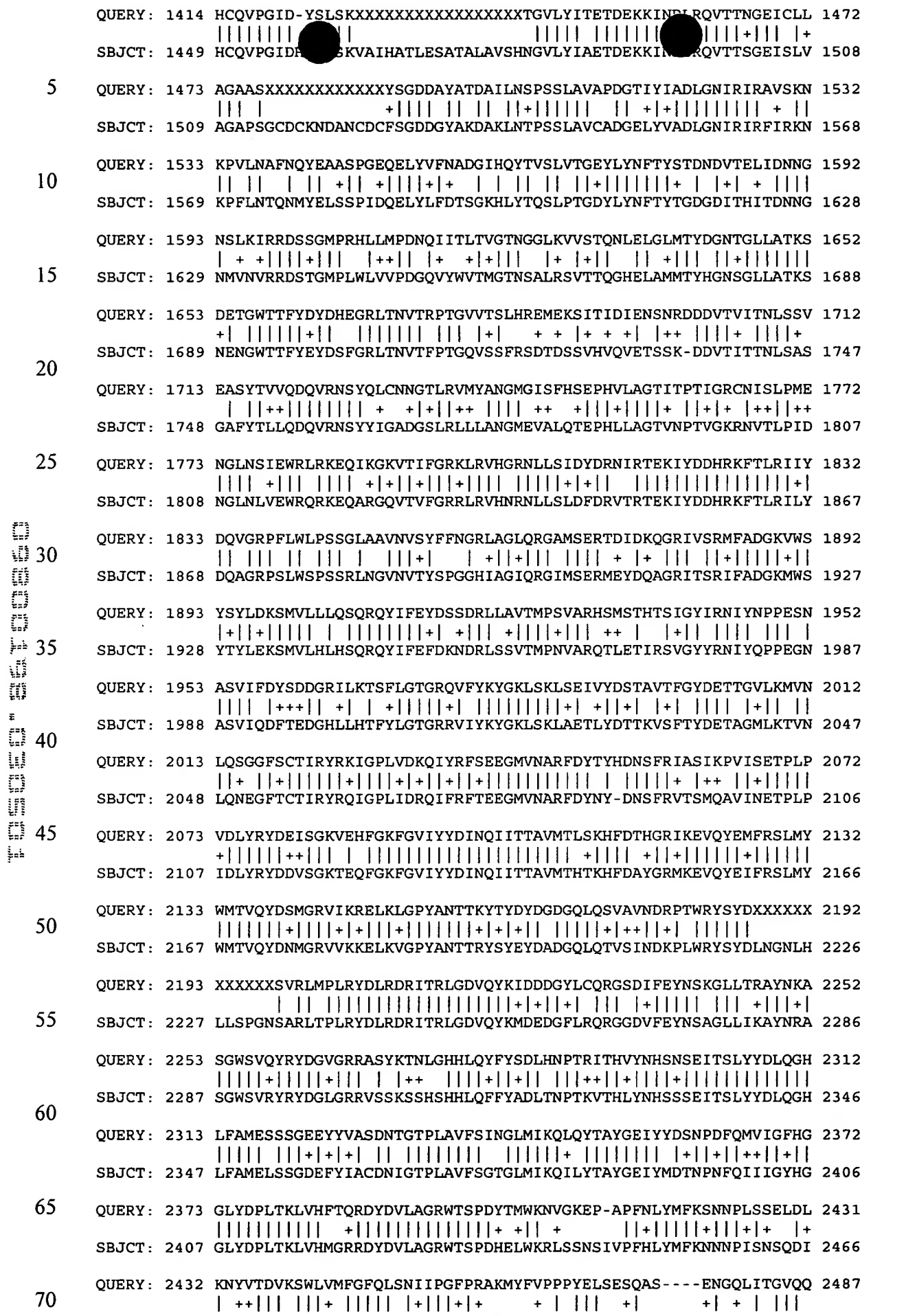


QUERY: 1414 HCQVPGID-YSLSKXXXXXXXXXXXXXXXXTGVLYITETDEKKINDLRQVTTNGEICLL 1472
SBJCT: 1449 HCQVPGIDH[redacted]SKVAIHATLESATALAVSHNGVLYIAETDEKKIN[redacted]RQVTTSGEISLV 1508

QUERY: 1473 AGAASXXXXXXXXXXXYSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKN 1532
SBJCT: 1509 AGAPSGCDCKNDANCDCFSGDDGYAKDAKLNTPSSLAVCADGELYVADLGNIRIRFIRKN 1568

QUERY: 1533 KPVLNAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELIDNNG 1592
SBJCT: 1569 KPFLNTQNMYELSSPIDQELYLFDTSGKHLYTQSLPTGDYLYNFTYTGDGDITHITDNNG 1628

QUERY: 1593 NSLKIRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNLELGLMTYDGNTGLLATKS 1652
SBJCT: 1629 NMVNVRRDSTGMPLWLVVPDGQVYWVTMGTNSALRSVTTQGHELAMMTYHGNSGLLATKS 1688

QUERY: 1653 DETGWTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNRDDDVTVITNLSSV 1712
SBJCT: 1689 NENGWTTFYEYDSFGRLTNVTFPTGQVSSFRSDTDSSVHVQVETSSK-DDVTITTNLSAS 1747

QUERY: 1713 EASYTVVQDQVRNSYQLCNNGTLRVMYANGMGISFHSEPHVLAGTITPTIGRCNISLPME 1772
SBJCT: 1748 GAFYTLLQDQVRNSYYIGADGSLRLLLANGMEVALQTEPHLLAGTVNPTVGKRNVTLPID 1807

QUERY: 1773 NGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLRIIY 1832
SBJCT: 1808 NGLNLVEWRQRKEQARGQVTVFGRRLRVHNRNLLSLDFDRVTRTEKIYDDHRKFTLRILY 1867

QUERY: 1833 DQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGRIVSRMFADGKVWS 1892
SBJCT: 1868 DQAGRPSLWSPSSRLNGVNVTYSPGGHIAGIQRGIMSERMEYDQAGRITSRIFADGKMWS 1927

QUERY: 1893 YSYLDKSMVLLLQSQRQYIFEYDSSDRLLAVTMPSVARHSMSTHTSIGYIRNIYNPPESN 1952
SBJCT: 1928 YTYLEKSMVLHLHSQRQYIFEFDKNDRLSSVTMPNVARQTLETIRSVGYYRNIYQPPEGN 1987

QUERY: 1953 ASVIFDYSDDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMVN 2012
SBJCT: 1988 ASVIQDFTEDGHLLHTFYLGTGRRVIYKYGKLSKLAETLYDTTKVSFTYDETAGMLKTVN 2047

QUERY: 2013 LQSGGFSCTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLP 2072
SBJCT: 2048 LQNEGFTCTIRYRQIGPLIDRQIFRFTEEGMVNARFDYNY-DNSFRVTSMQAVINETPLP 2106

QUERY: 2073 VDLYRYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFRSLMY 2132
SBJCT: 2107 IDLYRYDDVSGKTEQFGKFGVIYYDINQIITTAVMTHTKHFDAYGRMKEVQYEIFRSLMY 2166

QUERY: 2133 WMTVQYDSMGRVIKRELKLGPYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDXXXXXX 2192
SBJCT: 2167 WMTVQYDNMGRVVKKELKVGPYANTTRYSYEYDADGQLQTVSINDKPLWRYSYDLNGNLH 2226

QUERY: 2193 XXXXXXSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEYNSKGLLTRAYNKA 2252
SBJCT: 2227 LLSPGNSARLTPLRYDLRDRITRLGDVQYKMDEDGFLRQRGGDVFEYNSAGLLIKAYNRA 2286

QUERY: 2253 SGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGH 2312
SBJCT: 2287 SGWSVRYRYDGLGRRVSSKSSHSHHLQFFYADLTNPTKVTHLYNHSSSEITSLYYDLQGH 2346

QUERY: 2313 LFAMESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHG 2372
SBJCT: 2347 LFAMELSSGDEFYIACDNIGTPLAVFSGTGLMIKQILYTAYGEIYMDTNPNFQIIIGYHG 2406

QUERY: 2373 GLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEP-APFNLYMFKSNNPLSSELDL 2431
SBJCT: 2407 GLYDPLTKLVHMGRRDYDVLAGRWTSPDHELWKRLSSNSIVPFHLYMFKNNNPISNSQDI 2466

QUERY: 2432 KNYVTDVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQAS----ENGQLITGVQQ 2487

```
SBJCT: 2467 KCFMTDVNSWLLTFGFQLHNVIPGYPKPDTDAMEPSYELVHTQMKTGFWDNSKSILGVQC 2526

QUERY: 2488 TTERHNQAF  E------GQVITKKLHASIREKAGHWFATTTPI  GIMFAIKEGRVT 2541
              ++  +||+ ||      |  ||    |   +|    ||++  | |||+ ||+|+||||
SBJCT: 2527 EVQKQLKAFVTLERFDQLYGSTITSCQQAPETKK----FASSGSIFGKGVKFALKDGRVT 2582

QUERY: 2542 TGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYFVKIGSADGDLVTLGTTIGRKV 2601
            | + |+|+|| |++|++|||||+||+ +|++|+| ||||||| | ++|||  || + ||+
SBJCT: 2583 TDIISVANEDGRRIAAILNNAHYLENLHFTIDGVDTHYFVKPGPSEGDLAILGLSGGRRT 2642

QUERY: 2602 LESGVNVTVSQPTLLVNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQARQR 2661
            ||+|||||||||   +++|||||+|+|+ ||  | |+ |||    |+|||| |||+ ||||
SBJCT: 2643 LENGVNVTVSQINTMLSGRTRRYTDIQLQYRALCLNTRYG---TTVDEEKVRVLELARQR 2699

QUERY: 2662 ALGTAWAKEQQKARDGREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSN 2721
            |+  |||+|||+ |+| || | ||+|||||+|+|||||||+|++|  |||||||+||++|
SBJCT: 2700 AVRQAWAREQQRLREGEEGLRAWTDGEKQQVLNTGRVQGYDGFFVTSVEQYPELSDSANN 2759

QUERY: 2722 IQFLRQNEMGKR 2733
            | |+||+|||+|
SBJCT: 2760 IHFMRQSEMGRR 2771

 SCORE =  161 BITS (407), EXPECT = 2E-37
 IDENTITIES = 93/157 (59%), POSITIVES = 118/157 (74%), GAPS = 4/157 (2%)

QUERY: 1   MDVKDRR-HRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGN 59
           ||||+|+ +|||||  |   | ||||,|| |||+ + | ||||||||||||| |+|+ ||+
SBJCT: 1   MDVKERKPYRSLTRRR-DAERRYTSSSADSEEGKGP-QKSYSSSETLKAYDQDARLAYGS 58

QUERY: 60  RVTDLIHRESDEFPRQGTNFTLAELGICEPS-PHRSGYCSDMGILHQGYSLSTGSDADSD 118
           || |++ +|++|| | |||||| |||+ | + || + | +|+|+ | |||+   |||| +
SBJCT: 59  RVKDMVPQEAEEFCRTGTNFTLRELGLGEMTPPHGTLYRTDIGLPHCGYSMGASSDADLE 118

QUERY: 119 TEGGMSPEHAIRLWGRGIKSRRSSGLSSRENSALTLT 155
            +  +|||| +|||||  +| ||| |||| || ||||
SBJCT: 119 ADTVLSPEHPVRLWGRSTRSGRSSCLSSRANSNLTLT 155

 SCORE = 72.1 BITS (176), EXPECT = 8E-11
 IDENTITIES = 59/152 (38%), POSITIVES = 68/152 (43%), GAPS = 42/152 (27%)

QUERY: 285 PAPAPND--LATTP------ESVQLQDSWVLNSNVPLETR------------------- 316
           |+||| |  |+  |       |    ||+|+||||+|||||
SBJCT: 211 PSPAPTDHSLSGEPPAGSAQEPTHAQDNWLLNSNIPLETRNLGKQPFLGTLQDNLIEMDI 270

QUERY: 317 -------------HFLFKXXXXXXXXXXXXXXXYPLTSGTVYTPPPRLLPRNTFSRKAFK 363
                        |||||                |||||  |||+|||| |||+|||| ||
SBJCT: 271 LSASRHDGAYSDGHFLFK-PGGTSPLFCTTSPGYPLTSSTVYSPPPRPLPRSTFSRPAFN 329

QUERY: 364 LKKPSKYCSWKCXXXXXXXXXXXXXXXXXYFI 395
           ||||||||+|||                  ||+
SBJCT: 330 LKKPSKYCNWKCAALSAILISATLVILLAYFV 361

*FCTR3F DOES NOT CONTAIN THESE AMINO ACIDS
```

The 997-2733 amino acid fragment of the FCTR3bcde and f protein was also found to have 1695 of 1737 amino acid residues (97%) identical to, and 1695 of 1737 residues (97%) positive with the amino a 1737 amino acid residue protein KIAA1127 protein [*Homo sapiens*] (GenBank Acc:(AB032953) (SEQ ID NO:71), (Table 3S).

Table 3S. BLASTP of FCTR3b, c, d, e, and f against *Homo sapiens* KIAA1127 protein (SEQ ID NO:71)

```
>GI|6329763|DBJ|BAA86441.1| (AB032953) KIAA1127 PROTEIN [HOMO SAPIENS]
          LENGTH = 1737
```

SCORE = 3295 BITS (8545), EXPECT = 0.0
IDENTITIES = 1695/1 97%), POSITIVES = 1695/1737 (97%

```
QUERY: 997  TFFSAAPGQNPIVPETQVLHEEIELPGSNVKLRYLSSRTAGYKSLLKITMTQSTVPLNLI 1056
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1    TFFSAAPGQNPIVPETQVLHEEIELPGSNVKLRYLSSRTAGYKSLLKITMTQSTVPLNLI 60

QUERY: 1057 RVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLSDAVVSVGFEYETCPSLI 1116
            |||||||||||||||||||||||| ||||||||||||||||||||||||||||||||||||
SBJCT: 61   RVHLMVAVEGHLFQKSFQASPNLAYTFIWDKTDAYGQRVYGLSDAVVSVGFEYETCPSLI 120

QUERY: 1117 LWEKRTALLQGFELDPSNLGGWSLDKHHILNVKSGILHKGTGENQFLTQQPAIITSIMGN 1176
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 121  LWEKRTALLQGFELDPSNLGGWSLDKHHILNVKSGILHKGTGENQFLTQQPAIITSIMGN 180

QUERY: 1177 GRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIRRIFPSRNVTSILELRNK 1236
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 181  GRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIRRIFPSRNVTSILELRNK 240

QUERY: 1237 EFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGEQCL 1296
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 241  EFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGEQCL 300

QUERY: 1297 PFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTA 1356
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 301  PFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTA 360

QUERY: 1357 VRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSIIAGRPMHCQ 1416
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 361  VRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSIIAGRPMHCQ 420

QUERY: 1417 VPGIDYSLSKXXXXXXXXXXXXXXXXXTGVLYITETDEKKINRLRQVTTNGEICLLAGAA 1476
            ||||||||||                 ||||||||||||||||||||||||||||||||
SBJCT: 421  VPGIDYSLSKLAIHSALESASAIAISHTGVLYITETDEKKINRLRQVTTNGEICLLAGAA 480

QUERY: 1477 SXXXXXXXXXXXXYSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVL 1536
            |           ||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 481  SDCDCKNDVNCNCYSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVL 540

QUERY: 1537 NAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELIDNNGNSLK 1596
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 541  NAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELIDNNGNSLK 600

QUERY: 1597 IRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNLELGLMTYDGNTGLLATKSDETG 1656
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 601  IRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNLELGLMTYDGNTGLLATKSDETG 660

QUERY: 1657 WTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNRDDDVTVITNLSSVEASY 1716
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 661  WTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNRDDDVTVITNLSSVEASY 720

QUERY: 1717 TVVQDQVRNSYQLCNNGTLRVMYANGMGISFHSEPHVLAGTITPTIGRCNISLPMENGLN 1776
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 721  TVVQDQVRNSYQLCNNGTLRVMYANGMGISFHSEPHVLAGTITPTIGRCNISLPMENGLN 780

QUERY: 1777 SIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLRIIYDQVG 1836
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 781  SIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLRIIYDQVG 840

QUERY: 1837 RPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGRIVSRMFADGKVWSYSYL 1896
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 841  RPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGRIVSRMFADGKVWSYSYL 900

QUERY: 1897 DKSMVLLLQSQRQYIFEYDSSDRLLAVTMPSVARHSMSTHTSIGYIRNIYNPPESNASVI 1956
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 901  DKSMVLLLQSQRQYIFEYDSSDRLLAVTMPSVARHSMSTHTSIGYIRNIYNPPESNASVI 960

QUERY: 1957 FDYSDDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMVNLQSG 2016
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 961  FDYSDDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMVNLQSG 1020
```

```
QUERY: 2017 GFSCTIRY[redacted]PLVDKQIYRFSEEGMVNARFDYTYHDNSFRIA[redacted]VISETPLPVDLY 2076
           ||||||||[redacted]||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1021 GFSCTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLPVDLY 1080

QUERY: 2077 RYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTV 2136
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1081 RYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTV 1140

QUERY: 2137 QYDSMGRVIKRELKLGPYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDXXXXXXXXXX 2196
           ||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1141 QYDSMGRVIKRELKLGPYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDLNGNLHLLNP 1200

QUERY: 2197 XXSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEYNSKGLLTRAYNKASGWS 2256
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1201 GNSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEYNSKGLLTRAYNKASGWS 1260

QUERY: 2257 VQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGHLFAM 2316
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1261 VQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGHLFAM 1320

QUERY: 2317 ESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHGGLYD 2376
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1321 ESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHGGLYD 1380

QUERY: 2377 PLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEPAPFNLYMFKSNNPLSSELDLKNYVT 2436
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1381 PLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEPAPFNLYMFKSNNPLSSELDLKNYVT 1440

QUERY: 2437 DVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQAF 2496
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1441 DVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQAF 1500

QUERY: 2497 MALEGQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGRVTTGVSSIASEDSRKVA 2556
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1501 MALEGQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGRVTTGVSSIASEDSRKVA 1560

QUERY: 2557 SVLNNAYYLDKMHYSIEGKDTHYFVKIGSADGDLVTLGTTIGRKVLESGVNVTVSQPTLL 2616
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1561 SVLNNAYYLDKMHYSIEGKDTHYFVKIGSADGDLVTLGTTIGRKVLESGVNVTVSQPTLL 1620

QUERY: 2617 VNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQARQRALGTAWAKEQQKARD 2676
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1621 VNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQARQRALGTAWAKEQQKARD 1680

QUERY: 2677 GREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNEMGKR 2733
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1681 GREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNEMGKR 1737
```

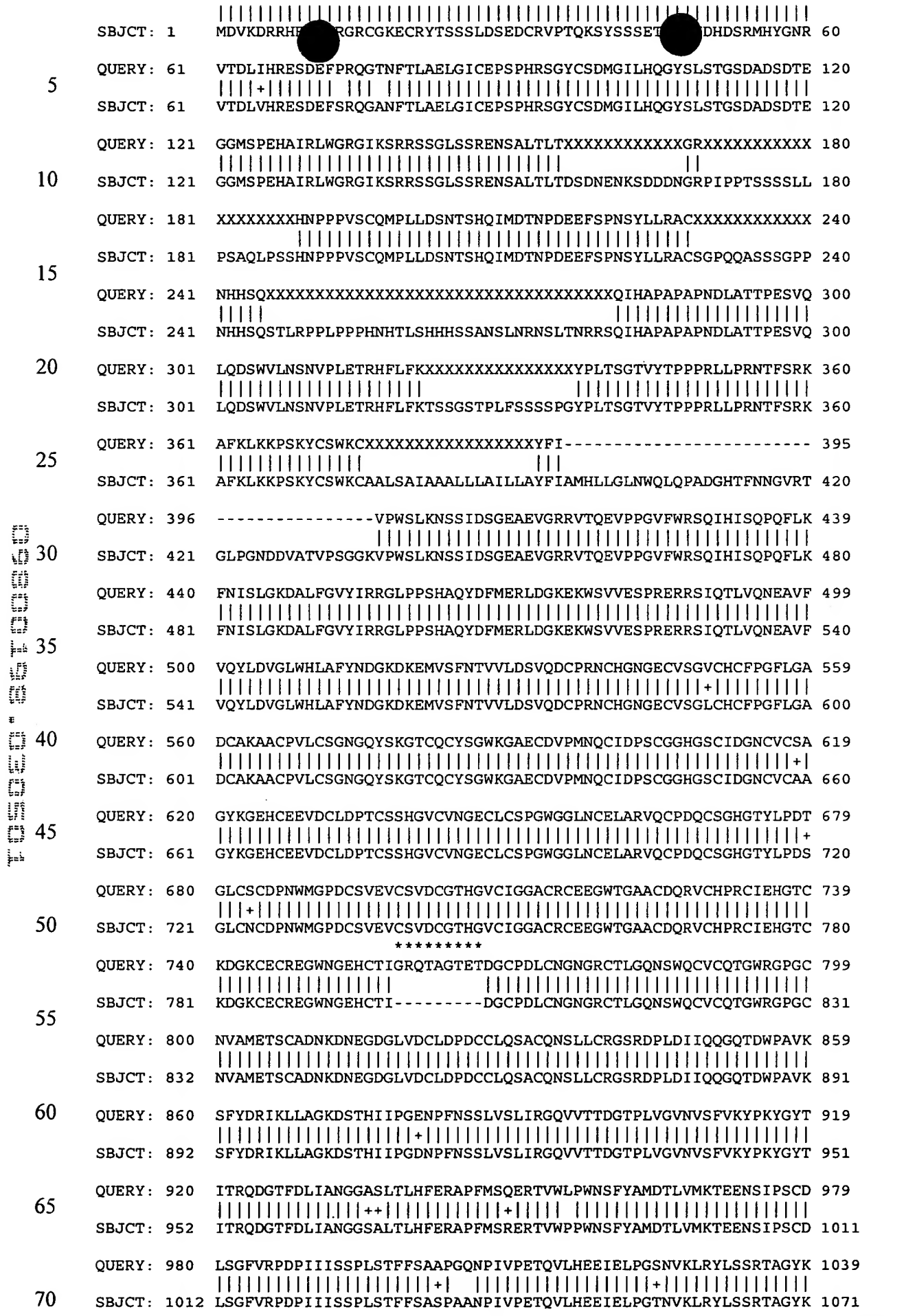
The amino acid sequences of the FCTR3bcde and f proteins were also found to have 2528 of 2774 amino acid residues (91%) identical to, and 2557 of 2774 residues (92%) positive with, the 2765 amino acid residue protein neurestin alpha [*Rattus norvegicus*] (GenBank Acc:AF086607) (SEQ ID NO:72), shown in Table 3T.

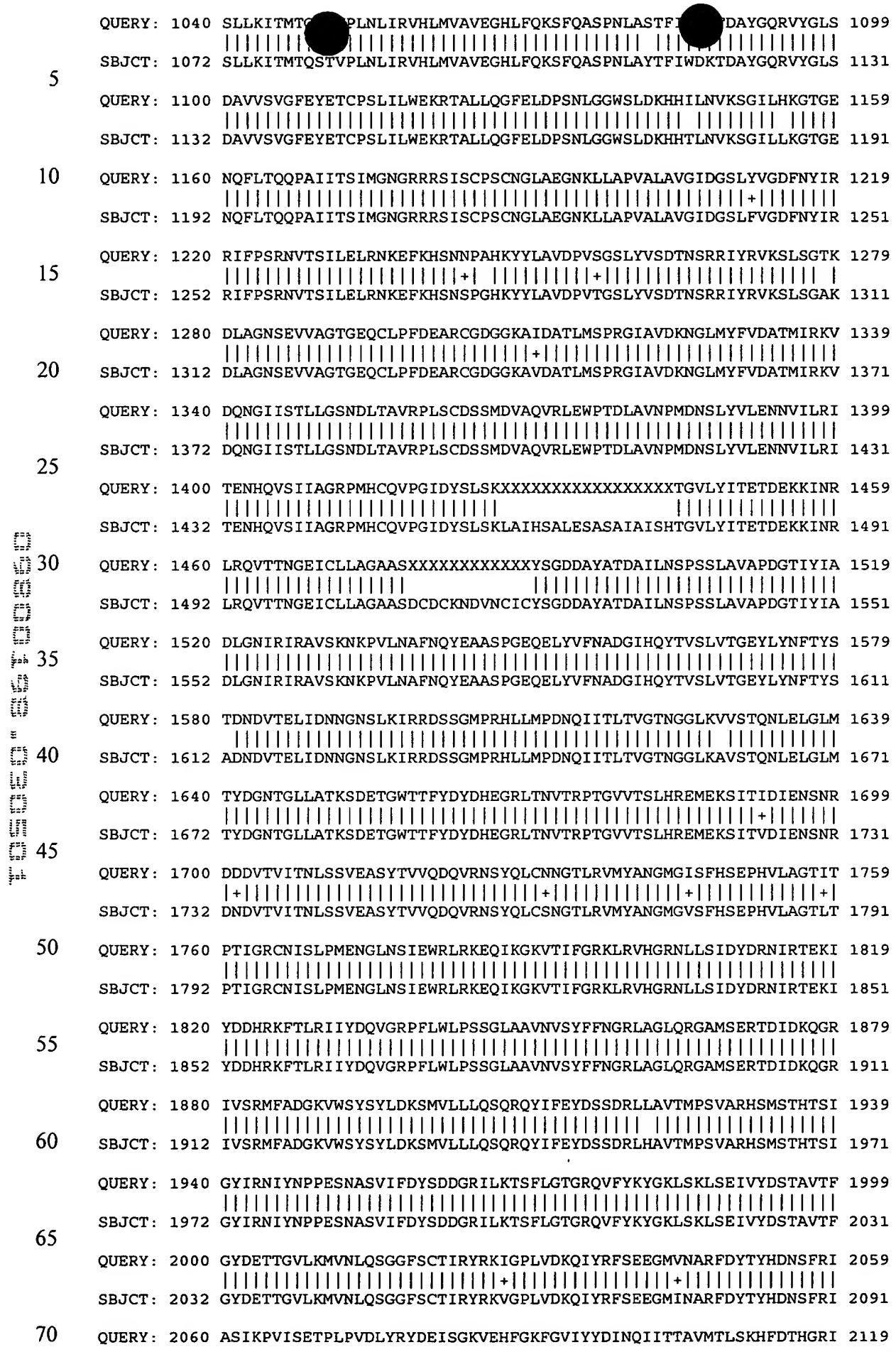
Table 3T. BLASTP of FCTR3bcd and f against *Rattus norvegicus* Neurestin alpha (SEQ ID NO:72)

```
>GI|9910320|REF|NP_064473.1| NEURESTIN ALPHA [RATTUS NORVEGICUS]
 GI|5712201|GB|AAD47383.1|AF086607_1 (AF086607) NEURESTIN ALPHA [RATTUS NORVEGICUS]
          LENGTH = 2765

 SCORE = 4988 BITS (12938), EXPECT = 0.0
 IDENTITIES = 2528/2774 (91%), POSITIVES = 2557/2774 (92%), GAPS = 50/2774 (1%)

QUERY: 1    MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNR 60
```


SBJCT: 1 MDVKDRRHF RGRCGKECRYTSSSLDSEDCRVPTQKSYSSSET DHDSRMHYGNR 60
QUERY: 61 VTDLIHRESDEFPRQGTNFTLAELGICEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTE 120
SBJCT: 61 VTDLVHRESDEFSRQGANFTLAELGICEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTE 120
QUERY: 121 GGMSPEHAIRLWGRGIKSRRSSGLSSRENSALTLTXXXXXXXXXXXXGRXXXXXXXXXXX 180
SBJCT: 121 GGMSPEHAIRLWGRGIKSRRSSGLSSRENSALTLTDSDNENKSDDDNGRPIPPTSSSSLL 180
QUERY: 181 XXXXXXXXHNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACXXXXXXXXXXXX 240
SBJCT: 181 PSAQLPSSHNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPP 240
QUERY: 241 NHHSQXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXQIHAPAPAPNDLATTPESVQ 300
SBJCT: 241 NHHSQSTLRPPLPPPHNHTLSHHHSSANSLNRNSLTNRRSQIHAPAPAPNDLATTPESVQ 300
QUERY: 301 LQDSWVLNSNVPLETRHFLFKXXXXXXXXXXXXXXXXYPLTSGTVYTPPPRLLPRNTFSRK 360
SBJCT: 301 LQDSWVLNSNVPLETRHFLFKTSSGSTPLFSSSSPGYPLTSGTVYTPPPRLLPRNTFSRK 360
QUERY: 361 AFKLKKPSKYCSWKCXXXXXXXXXXXXXXXXXYFI---------- 395
SBJCT: 361 AFKLKKPSKYCSWKCAALSAIAAALLLAILLAYFIAMHLLGLNWQLQPADGHTFNNGVRT 420
QUERY: 396 ----------VPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQIHISQPQFLK 439
SBJCT: 421 GLPGNDDVATVPSGGKVPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQIHISQPQFLK 480
QUERY: 440 FNISLGKDALFGVYIRRGLPPSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVF 499
SBJCT: 481 FNISLGKDALFGVYIRRGLPPSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVF 540
QUERY: 500 VQYLDVGLWHLAFYNDGKDKEMVSFNTVVLDSVQDCPRNCHGNGECVSGVCHCFPGFLGA 559
SBJCT: 541 VQYLDVGLWHLAFYNDGKDKEMVSFNTVVLDSVQDCPRNCHGNGECVSGLCHCFPGFLGA 600
QUERY: 560 DCAKAACPVLCSGNGQYSKGTCQCYSGWKGAECDVPMNQCIDPSCGGHGSCIDGNCVCSA 619
SBJCT: 601 DCAKAACPVLCSGNGQYSKGTCQCYSGWKGAECDVPMNQCIDPSCGGHGSCIDGNCVCAA 660
QUERY: 620 GYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDT 679
SBJCT: 661 GYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDS 720
QUERY: 680 GLCSCDPNWMGPDCSVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTC 739
SBJCT: 721 GLCNCDPNWMGPDCSVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTC 780
****
QUERY: 740 KDGKCECREGWNGEHCTIGRQTAGTETDGCPDLCNGNGRCTLGQNSWQCVCQTGWRGPGC 799
SBJCT: 781 KDGKCECREGWNGEHCTI---------DGCPDLCNGNGRCTLGQNSWQCVCQTGWRGPGC 831
QUERY: 800 NVAMETSCADNKDNEGDGLVDCLDPDCCLQSACQNSLLCRGSRDPLDIIQQGQTDWPAVK 859
SBJCT: 832 NVAMETSCADNKDNEGDGLVDCLDPDCCLQSACQNSLLCRGSRDPLDIIQQGQTDWPAVK 891
QUERY: 860 SFYDRIKLLAGKDSTHIIPGENPFNSSLVSLIRGQVVTTDGTPLVGVNVSFVKYPKYGYT 919
SBJCT: 892 SFYDRIKLLAGKDSTHIIPGDNPFNSSLVSLIRGQVVTTDGTPLVGVNVSFVKYPKYGYT 951
QUERY: 920 ITRQDGTFDLIANGGASLTLHFERAPFMSQERTVWLPWNSFYAMDTLVMKTEENSIPSCD 979
SBJCT: 952 ITRQDGTFDLIANGGSALTLHFERAPFMSRERTVWPPWNSFYAMDTLVMKTEENSIPSCD 1011
QUERY: 980 LSGFVRPDPIIISSPLSTFFSAAPGQNPIVPETQVLHEEIELPGSNVKLRYLSSRTAGYK 1039
SBJCT: 1012 LSGFVRPDPIIISSPLSTFFSASPAANPIVPETQVLHEEIELPGTNVKLRYLSSRTAGYK 1071


QUERY: 1040 SLLKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLS 1099
SBJCT: 1072 SLLKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLAYTFIWDKTDAYGQRVYGLS 1131
QUERY: 1100 DAVVSVGFEYETCPSLILWEKRTALLQGFELDPSNLGGWSLDKHHILNVKSGILHKGTGE 1159
SBJCT: 1132 DAVVSVGFEYETCPSLILWEKRTALLQGFELDPSNLGGWSLDKHHTLNVKSGILLKGTGE 1191
QUERY: 1160 NQFLTQQPAIITSIMGNGRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIR 1219
SBJCT: 1192 NQFLTQQPAIITSIMGNGRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLFVGDFNYIR 1251
QUERY: 1220 RIFPSRNVTSILELRNKEFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTK 1279
SBJCT: 1252 RIFPSRNVTSILELRNKEFKHSNSPGHKYYLAVDPVTGSLYVSDTNSRRIYRVKSLSGAK 1311
QUERY: 1280 DLAGNSEVVAGTGEQCLPFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKV 1339
SBJCT: 1312 DLAGNSEVVAGTGEQCLPFDEARCGDGGKAVDATLMSPRGIAVDKNGLMYFVDATMIRKV 1371
QUERY: 1340 DQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRI 1399
SBJCT: 1372 DQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRI 1431
QUERY: 1400 TENHQVSIIAGRPMHCQVPGIDYSLSKXXXXXXXXXXXXXXXXXTGVLYITETDEKKINR 1459
SBJCT: 1432 TENHQVSIIAGRPMHCQVPGIDYSLSKLAIHSALESASAIAISHTGVLYITETDEKKINR 1491
QUERY: 1460 LRQVTTNGEICLLAGAASXXXXXXXXXXXXYSGDDAYATDAILNSPSSLAVAPDGTIYIA 1519
SBJCT: 1492 LRQVTTNGEICLLAGAASDCDCKNDVNCICYSGDDAYATDAILNSPSSLAVAPDGTIYIA 1551
QUERY: 1520 DLGNIRIRAVSKNKPVLNAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYS 1579
SBJCT: 1552 DLGNIRIRAVSKNKPVLNAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYS 1611
QUERY: 1580 TDNDVTELIDNNGNSLKIRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNLELGLM 1639
SBJCT: 1612 ADNDVTELIDNNGNSLKIRRDSSGMPRHLLMPDNQIITLTVGTNGGLKAVSTQNLELGLM 1671
QUERY: 1640 TYDGNTGLLATKSDETGWTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNR 1699
SBJCT: 1672 TYDGNTGLLATKSDETGWTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITVDIENSNR 1731
QUERY: 1700 DDDVTVITNLSSVEASYTVVQDQVRNSYQLCNNGTLRVMYANGMGISFHSEPHVLAGTIT 1759
SBJCT: 1732 DNDVTVITNLSSVEASYTVVQDQVRNSYQLCSNGTLRVMYANGMGVSFHSEPHVLAGTLT 1791
QUERY: 1760 PTIGRCNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKI 1819
SBJCT: 1792 PTIGRCNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKI 1851
QUERY: 1820 YDDHRKFTLRIIYDQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGR 1879
SBJCT: 1852 YDDHRKFTLRIIYDQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGR 1911
QUERY: 1880 IVSRMFADGKVWSYSYLDKSMVLLLQSQRQYIFEYDSSDRLLAVTMPSVARHSMSTHTSI 1939
SBJCT: 1912 IVSRMFADGKVWSYSYLDKSMVLLLQSQRQYIFEYDSSDRLHAVTMPSVARHSMSTHTSI 1971
QUERY: 1940 GYIRNIYNPPESNASVIFDYSDDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTF 1999
SBJCT: 1972 GYIRNIYNPPESNASVIFDYSDDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTF 2031
QUERY: 2000 GYDETTGVLKMVNLQSGGFSCTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRI 2059
SBJCT: 2032 GYDETTGVLKMVNLQSGGFSCTIRYRKVGPLVDKQIYRFSEEGMINARFDYTYHDNSFRI 2091
QUERY: 2060 ASIKPVISETPLPVDLYRYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRI 2119

```
SBJCT: 2092 ASIKPVIS[redacted]PVDLYRYDEISGKVEHFGKFGVIYYDINQIITT[redacted]LSKHFDTHGRI 2151

QUERY: 2120 KEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGPYANTTKYTYDYDGDGQLQSVAVNDRP 2179
SBJCT: 2152 KEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGPYANTTKYTYDYDGDGQLQSVAVNDRP 2211

QUERY: 2180 TWRYSYDXXXXXXXXXXXXSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEY 2239
SBJCT: 2212 TWRYSYDLNGNLHLLNPGNSARLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEY 2271

QUERY: 2240 NSKGLLTRAYNKASGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSN 2299
SBJCT: 2272 NSKGLLTRAYNKASGWSVQYRYDGVSRRASYKTNLGHHLQYFYSDLHHPTRITHVYNHSN 2331

QUERY: 2300 SEITSLYYDLQGHLFAMESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYD 2359
SBJCT: 2332 SEITSLYYDLQGHLFAMESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYD 2391

QUERY: 2360 SNPDFQMVIGFHGGLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEPAPFNLYMF 2419
SBJCT: 2392 SNPDFQMVIGFHGGLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWRNVGKEPAPFNLYMF 2451

QUERY: 2420 KSNNPLSSELDLKNYVTDVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENG 2479
SBJCT: 2452 KNNNPLSNELDLKNYVTDVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENG 2511

QUERY: 2480 QLITGVQQTTERHNQAFMALEGQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGR 2539
SBJCT: 2512 QLITGVQQTTERHNQAFLALEGQVISKKLHAGIREKAGHWFATTTPIIGKGIMFAIKEGR 2571

QUERY: 2540 VTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYFVKIGSADGDLVTLGTTIGR 2599
SBJCT: 2572 VTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYFVKIGAADGDLVTLGTTIGR 2631

QUERY: 2600 KVLESGVNVTVSQPTLLVNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQAR 2659
SBJCT: 2632 KVLESGVNVTVSQPTLLVNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQAR 2691

QUERY: 2660 QRALGTAWAKEQQKARDGREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSS 2719
SBJCT: 2692 QRALGTAWAKEQQKARDGREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSS 2751

QUERY: 2720 SNIQFLRQNEMGKR 2733
SBJCT: 2752 SNIQFLRQNEMGKR 2765

* = FCTR3F DOES NOT CONTAIN THESE AMINO ACIDS
```

The amino acid sequences of the FCTR3bcde and f proteins were also found to have 2536 of 2774 amino acid residues (91%) identical to, and 2558 of 2774 residues (91%) positive with, the 2764 amino acid residue protein Odd Oz/ten-m homolog 2 (*Drosophila*) (GenBank Acc:NP_035986.2) (SEQ ID NO:65), shown in Table 3U.

Table 3U. BLASTP of FCTR3bcde and f against Odd Oz/ten-m homolog 2 (SEQ ID NO:65)

```
>GI|7657415|REF|NP_035986.2| ODD OZ/TEN-M HOMOLOG 2 (DROSOPHILA); ODD OZ/TEN-M HOMOLOG
3
            (DROSOPHILA) [MUS MUSCULUS]
 GI|4760778|DBJ|BAA77397.1| (AB025411) TEN-M2 [MUS MUSCULUS]
          LENGTH = 2764

 SCORE = 4996 BITS (12961), EXPECT = 0.0
```

```
 IDENTITIES = 2536/2774 (91%), POSITIVES = 2558/2774 (91%), GAPS = 51/2774 (1%)

QUERY: 1    MDVKDRRH[redacted]RGRCGKECRYTSSSLDSEDCRVPTQKSYSSSET[redacted]YDHDSRMHYGNR 60
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1    MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNR 60

QUERY: 61   VTDLIHRESDEFPRQGTNFTLAELGICEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTE 120
            ||||+|||||||| ||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 61   VTDLVHRESDEFSRQGTNFTLAELGICEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTE 120

QUERY: 121  GGMSPEHAIRLWGRGIKSRRSSGLSSRENSALTLTXXXXXXXXXXXXGRXXXXXXXXXXX 180
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 121  GGMSPEHAIRLWGRGIKSRRSSGLSSRENSALTLTDSDNENKSDDDNGRPIPPTSSSSLL 180

QUERY: 181  XXXXXXXXHNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACXXXXXXXXXXXX 240
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 181  PSAQLPSSHNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPP 240

QUERY: 241  NHHSQXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXQIHAPAPAPNDLATTPESVQ 300
            |||||                                    ||||||||||||||||||||
SBJCT: 241  NHHSQSTLRPPLPPPHNHTLSHHHSSANSLNRNSLTNRRSQIHAPAPAPNDLATTPESVQ 300

QUERY: 301  LQDSWVLNSNVPLETRHFLFKXXXXXXXXXXXXXXXXYPLTSGTVYTPPPRLLPRNTFSRK 360
            |||||||||||||||||||                ||||||||||||||||||||||||
SBJCT: 301  LQDSWVLNSNVPLETRHFLFKTSSGSTPLFSSSSPGYPLTSGTVYTPPPRLLPRNTFSRK 360

QUERY: 361  AFKLKKPSKYCSWKCXXXXXXXXXXXXXXXXXYFI------------------------ 395
            ||||||||||||||||                   |||
SBJCT: 361  AFKLKKPSKYCSWKCAALSAIAAALLLAILLAYFIAMHLLGLNWQLQPADGHTFNNGVRT 420

QUERY: 396  ----------------VPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQIHISQPQFLK 439
                            ||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 421  GLPGNDDVATVPSGGKVPWSLKNSSIDSGEAEVGRRVTQEVPPGVFWRSQIHISQPQFLK 480

QUERY: 440  FNISLGKDALFGVYIRRGLPPSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVF 499
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 481  FNISLGKDALFGVYIRRGLPPSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVF 540

QUERY: 500  VQYLDVGLWHLAFYNDGKDKEMVSFNTVVLDSVQDCPRNCHGNGECVSGVCHCFPGFLGA 559
            ||||||||||||||||||||||||||||||||||||||||||||||||||+|||||||||||
SBJCT: 541  VQYLDVGLWHLAFYNDGKDKEMVSFNTVVLDSVQDCPRNCHGNGECVSGLCHCFPGFLGA 600

QUERY: 560  DCAKAACPVLCSGNGQYSKGTCQCYSGWKGAECDVPMNQCIDPSCGGHGSCIDGNCVCSA 619
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||+|
SBJCT: 601  DCAKAACPVLCSGNGQYSKGTCQCYSGWKGAECDVPMNQCIDPSCGGHGSCIDGNCVCAA 660

QUERY: 620  GYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDT 679
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||+
SBJCT: 661  GYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDS 720

QUERY: 680  GLCSCDPNWMGPDCSVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTC 739
            |||||||||||||||| ||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 721  GLCSCDPNWMGPDCSV-VCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTC 779
                            *********
QUERY: 740  KDGKCECREGWNGEHCTIGRQTAGTETDGCPDLCNGNGRCTLGQNSWQCVCQTGWRGPGC 799
            ||||||||||||||||||         ||||||||||||||||||||||||||||||||||
SBJCT: 780  KDGKCECREGWNGEHCTI---------DGCPDLCNGNGRCTLGQNSWQCVCQTGWRGPGC 830

QUERY: 800  NVAMETSCADNKDNEGDGLVDCLDPDCCLQSACQNSLLCRGSRDPLDIIQQGQTDWPAVK 859
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 831  NVAMETSCADNKDNEGDGLVDCLDPDCCLQSACQNSLLCRGSRDPLDIIQQGQTDWPAVK 890

QUERY: 860  SFYDRIKLLAGKDSTHIIPGENPFNSSLVSLIRGQVVTTDGTPLVGVNVSFVKYPKYGYT 919
            ||||||||||||||||||+|||||||||||||||| ||||||||||||||||||||||||
SBJCT: 891  SFYDRIKLLAGKDSTHIIPGDNPFNSSLVSLIRGQVVTMDGTPLVGVNVSFVKYPKYGYT 950

QUERY: 920  ITRQDGTFDLIANGGASLTLHFERAPFMSQERTVWLPWNSFYAMDTLVMKTEENSIPSCD 979
            ||||||||||||||++||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 951  ITRQDGTFDLIANGGSALTLHFERAPFMSQERTVWLPWNSFYAMDTLVMKTEENSIPSCD 1010
```


QUERY: 980 LSGFVRPDPIIISSPLSTFFSAAPGQNPIVPETQVLHEEIELPGSNFLRYLSSRTAGYK 1039
SBJCT: 1011 LSGFVRPD SSPLSTFFSASPASNPIVPETQVLHEEIELPGTN LRYLSSRTAGYK 1070
QUERY: 1040 SLLKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLS 1099
SBJCT: 1071 SLLKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLAYTFIWDKTDAYGQRVYGLS 1130
QUERY: 1100 DAVVSVGFEYETCPSLILWEKRTALLQGFELDPSNLGGWSLDKHHILNVKSGILHKGTGE 1159
SBJCT: 1131 DAVVSVGFEYETCPSLILWEKRTALLQGFELDPSNLGGWSLDKHHTLNVKSGILHKGTGE 1190
QUERY: 1160 NQFLTQQPAIITSIMGNGRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIR 1219
SBJCT: 1191 NQFLTQQPAIITSIMGNGRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLFVGDFNYIR 1250
QUERY: 1220 RIFPSRNVTSILELRNKEFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTK 1279
SBJCT: 1251 RIFPSRNVTSILELRNKEFKHSNSPGHKYYLAVDPVTGSLYVSDTNSRRIYRVKSLSGAK 1310
QUERY: 1280 DLAGNSEVVAGTGEQCLPFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKV 1339
SBJCT: 1311 DLAGNSEVVAGTGEQCLPFDEARCGDGGKAVDATLMSPRGIAVDKNGLMYFVDATMIRKV 1370
QUERY: 1340 DQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRI 1399
SBJCT: 1371 DQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRI 1430
QUERY: 1400 TENHQVSIIAGRPMHCQVPGIDYSLSKXXXXXXXXXXXXXXXXXTGVLYITETDEKKINR 1459
SBJCT: 1431 TENHQVSIIAGRPMHCQVPGIDYSLSKLAIHSALESASAIAISHTGVLYITETDEKKINR 1490
QUERY: 1460 LRQVTTNGEICLLAGAASXXXXXXXXXXXXYSGDDAYATDAILNSPSSLAVAPDGTIYIA 1519
SBJCT: 1491 LRQVTTNGEICLLAGAASDCDCKNDVNCICYSGDDAYATDAILNSPSSLAVAPDGTIYIA 1550
QUERY: 1520 DLGNIRIRAVSKNKPVLNAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYS 1579
SBJCT: 1551 DLGNIRIRAVSKNKPVLNAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYS 1610
QUERY: 1580 TDNDVTELIDNNGNSLKIRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNLELGLM 1639
SBJCT: 1611 ADNDVTELIDNNGNSLKIRRDSSGMPRHLLMPDNQIITLTVGTNGGLKAVSTQNLELGLM 1670
QUERY: 1640 TYDGNTGLLATKSDETGWTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNR 1699
SBJCT: 1671 TYDGNTGLLATKSDETGWTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNR 1730
QUERY: 1700 DDDVTVITNLSSVEASYTVVQDQVRNSYQLCNNGTLRVMYANGMGISFHSEPHVLAGTIT 1759
SBJCT: 1731 DDDVTVITNLSSVEASYTVVQDQVRNSYQLCNNGTLRVMYANGMAVSFHSEPHVLAGTIT 1790
QUERY: 1760 PTIGRCNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKI 1819
SBJCT: 1791 PTIGRCNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKI 1850
QUERY: 1820 YDDHRKFTLRIIYDQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGR 1879
SBJCT: 1851 YDDHRKFTLRIIYDQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGR 1910
QUERY: 1880 IVSRMFADGKVWSYSYLDKSMVLLLQSQRQYIFEYDSSDRLLAVTMPSVARHSMSTHTSI 1939
SBJCT: 1911 IVSRMFADGKVWSYSYLDKSMVLLLQSQRQYIFEYDSSDRLHAVTMPSVARHSMSTHTSI 1970
QUERY: 1940 GYIRNIYNPPESNASVIFDYSDDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTF 1999
SBJCT: 1971 GYIRNIYNPPESNASVIFDYSDDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTF 2030
QUERY: 2000 GYDETTGVLKMVNLQSGGFSCTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRI 2059

```
SBJCT: 2031 GYDETTGVLKMVNLQSGGFSCTIRYRKVGPLVDKQIYRFSEEGMINFFDYTYHDNSFRI 2090

QUERY: 2060 ASIKPVISE PVDLYRYDEISGKVEHFGKFGVIYYDINQIITTA TLSKHFDTHGRI 2119
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 2091 ASIKPVISETPLPVDLYRYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRI 2150

QUERY: 2120 KEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGPYANTTKYTYDYDGDGQLQSVAVNDRP 2179
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 2151 KEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGPYANTTKYTYDYDGDGQLQSVAVNDRP 2210

QUERY: 2180 TWRYSYDXXXXXXXXXXXXSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEY 2239
           |||||||           | ||||||||||||||||||||||||||||||||||||||
SBJCT: 2211 TWRYSYDLNGNLHLLNPGNSARLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEY 2270

QUERY: 2240 NSKGLLTRAYNKASGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSN 2299
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 2271 NSKGLLTRAYNKASGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSN 2330

QUERY: 2300 SEITSLYYDLQGHLFAMESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYD 2359
           ||||||||||||||||||||||||||||||||||||+||||||||||||||||||||||
SBJCT: 2331 SEITSLYYDLQGHLFAMESSSGEEYYVASDNTGTPLAVYSINGLMIKQLQYTAYGEIYYD 2390

QUERY: 2360 SNPDFQMVIGFHGGLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEPAPFNLYMF 2419
           ||||||||||||||||||||||||||||||||||||||||||||||||+|||||||||||||
SBJCT: 2391 SNPDFQMVIGFHGGLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWRNVGKEPAPFNLYMF 2450

QUERY: 2420 KSNNPLSSELDLKNYVTDVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENG 2479
           |+|||||+||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 2451 KNNNPLSNELDLKNYVTDVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENG 2510

QUERY: 2480 QLITGVQQTTERHNQAFMALEGQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGR 2539
           ||||||||||||||||+||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 2511 QLITGVQQTTERHNQAFLALEGQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGR 2570

QUERY: 2540 VTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYFVKIGSADGDLVTLGTTIGR 2599
           ||||||||||||||||||||||||||||||||||||||||||||||||+|||||||||||||
SBJCT: 2571 VTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYFVKIGAADGDLVTLGTTIGR 2630

QUERY: 2600 KVLESGVNVTVSQPTLLVNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQAR 2659
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 2631 KVLESGVNVTVSQPTLLVNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQAG 2690

QUERY: 2660 QRALGTAWAKEQQKARDGREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSS 2719
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 2691 QRALGTAWAKEQQKARDGREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSS 2750

QUERY: 2720 SNIQFLRQNEMGKR 2733
           ||||||||||||||
SBJCT: 2751 SNIQFLRQNEMGKR 2764

* = FCTR3F DOES NOT CONTAIN THESE AMINO ACIDS
```

FCTR3 is related to rat neurestin, a gene implicated in neuronal development (Otaki JM, Firestein S Dev Biol 1999 Aug 1;212(1):165-81) Neurestin shows homology to human gamma-heregulin, a Drosophila receptor-type pair-rule gene product, Odd Oz (Odz) / Ten(m), and Ten(a). Neurestin has putative roles in synapse formation and brain morphogenesis. A mouse neurestin homolog, DOC4, has independently been isolated from the NIH-3T3 fibroblasts. DOC4 is also known as tenascin M (TNM), a *Drosophila* pair-rule gene homolog containing extracellular EGF-like repeats. The significant homology to these molecules and in particular, γ-heregulin, have important implications regarding the potential contribution of FCTR3 to disease progression. Heregulin is the ligand for HER-2/ErbB2/NEU, a proto-oncogene receptor tyrosine

kinase implicated in breast and prostate cancer progression that was originally identified in rat neuro/glioblastoma cell lines. Extopic expression of HER-2/ErbB2/NEU in MDA-MB-435 breast adenocarcinoma cells confers chemoresistance to Taxol-induced apoptosis relative to vector transfected control cells (Yu et al. Overexpression of ErbB2 blocks Taxol-induced apoptosis by up-regulation of p21Cip1, which inhibits p34Cdc2 kinase. Molec. Cell 2: 581-591, 1998).

FCTR3 related tenascins and cancer biology

As mentioned, FCTR3 also has significant homology to DOC4, (AKA tenascin M), a *Drosophila* pair-rule gene homolog containing extracellular EGF-like repeats. The tenascins are a growing family of extracellular matrix proteins that play prominent roles in tissue interactions critical to embryogenesis. Overexpression of tenascins has been described in multiple human solid malignancies.

The role of the tenascin family of related proteins is to regulate epithelial-stromal interactions, participate in fibronectin-dependent cell attachment and interaction. Indeed, tenascin-C (TN) is overexpressed in the stroma of malignant ovarian tumours particularly at the interface between epithelia and stroma leading to suggestions that it may be involved in the process of invasion (Wilson et al (1996) Br J Cancer 74: 999-1004). Tenascin-C is considered a therapeutic target for certain malignant brain tumors (Gladson CL : J Neuropathol Exp Neurol 1999 Oct;58(10):1029-40). Stromal or moderate to strong periductal Tenascin-C expression in DCIS (ductal carcinoma in situ) correlates with tumor cell invasion. (Jahkola et al. Eur J Cancer 1998 Oct;34(11):1687-92. Tenascin-C expression at the invasion border of early breast cancer is a useful predictor of local and distant recurrence. Jahkola T, et al. Br J Cancer. 1998 Dec;78(11):1507-13). Tenascin (TN) is an extracellular matrix protein found in areas of cell migration during development and expressed at high levels in migratory glioma cells. Treasurywala S, Berens ME Glia 1998 Oct;24(2):236-43 Migration arrest in glioma cells is dependent on the alphaV integrin subunit. Phillips GR, Krushel LA, Crossin KL J Cell Sci 1998 Apr;111 (Pt 8):1095-104 Domains of tenascin involved in glioma migration. Finally, tenascin expression in hormone-dependent tissues of breast and endometrium indicate that Tenascin expression reflects malignant progression and is down-regulated by antiprogestins during terminal differentiation of rat mammary tumors (Vollmer et al. Cancer Res 1992 Sep 1;52(17):4642-8)

Potential role of FCTR3 in oncologic disease progression:

Based on the bioactivity described in the medical literature for related molecules, FCTR3 may play a role in one or more aspects of tumor cell biology that alter the interactions of tumor epithelial cells with stromal components. In consideration, FCTR3 may play a role in the following malignant properties:

Autocrine/paracrine stimulation of tumor cell proliferation

Autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy

Local tissue remodeling, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis.

Tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveilance.

Therapeutic intervention targeting FCTR3 in oncologic and central nervous system indications:

Predicted disease indications from expression profiling in 41 normal human tissues and 55 human cancer cell lines (see Example 2) include a subset of human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas. Targeting of FCTR3 by human or humanized monoclonal antibodies designed to disrupt predicted interactions of FCTR3 with its cognate ligand may result in significant anti-tumor/anti-metastatic activity and the amelioration of associated symptomatology. Identification of small molecules that specifically/selectively interfere with downstream signaling components engaged by FCTR3/ligandinteractions would also be expected to result in significant anti-tumor/anti-metastatic activity and the amelioration of associated symptomatology. Likewise, modified antisense ribonucleotides or antisense gene expression constructs (plasmids, adenovirus, adeno-associated viruses, "naked" DNA approaches) designed to diminish the expression of FCTR3 transcripts/messenger RNA (mRNA) would be anticipated based on predicted properties of FCTR3 to have anti-tumor impact.

Based on the relatedness to neurestin and heregulins, as well as its high level expression in brain tissue, FCTR3 may also be used for remyelination in order to promote regeneration/repair/remyleination of injured central nervous system cells resulting from ischemia, brain trauma and various neurodegenerative diseases.. This postulate is based on reports indicating that neuregulin, glial growth factor 2, diminishes autoimmune demyelination and enhances remyelination in a chronic relapsing model for multiple sclerosis (Cannella et al. .

Proc. Nat. Acad. Sci. 95: 10100-10105, 1998). The expression of the related molecule neurestin can be induced in external tufted cells during regeneration of olfactory sensory neurons.

FCTR4

FCTR4 is a plasma membrane protein related to NF-Kappa-B P65delta3 protein. The clone is expressed in fetal liver tissues.

The novel FCTR4 nucleic acid of 609 nucleotides (also referred to as 29692275.0.1) is shown in Table 4A. An ORF begins with an ATG initiation codon at nucleotides 99-101 and ends with a TAA codon at nucleotides 522-524. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 4A, and the start and stop codons are in bold letters.

Table 4A. FCTR4 Nucleotide Sequence (SEQ ID NO:14)

CTGACATACTATATTAGTTGTTTGTTCACTGTCTCCACTCCAGCTAGAATATAAGTTCCATAGGGCAGAGTTTTTGTTCA
CTGCTATATTTTATAAGC**ATG**AATGAATGCATGAACGAATGGACTGATAACCCACAAGCCAAAGACCTCCATGACCTGCC
ACTGCCCTCCTTTCATTTTATTCTCACCTCTACCAATACTAAATCACCTAGTTATGTAAATACGATATGCACTTTCATGG
CCCCTTGCTTTGTCATATGCTGTTCCCTTTGCCTGGAATATAAACTCTCAAAATACCATCCACATTTTAAAATCTTCTCC
AGAAAGCTTCCTCTGTCCACCCCCACCCTCCCACCCCCATATAGAGTAAGTCAGTCTTTCCTTTGTGCTACATTTGTACC
TGTATCTACAGTGGCTCTAATCAAACTGCACTGTGTCTCTCACTTCCTAGATTGTGAACTCTTTGAGGCTGAAGACTACT
TATTCATCTCTTTACCTCCAATGCCTAGGACAGGACCTTCA**TAA**AGCAACTACTCTATAAATGTTGAAACATATGCATGA
CTATTCTGTAACAGGAATGAAAATATGGCATTTCAAGAAGTCACTACTC

The FCTR4 protein encoded by SEQ ID NO:14 has 141 amino acid residues and is presented using the one-letter code in Table 4B. The Psort profile for FCTR4 predicts that this sequence has no N-terminal signal peptide and is likely to be localized at the plasma membrane with a certainty of 0.6000. The most likely cleavage site for a peptide is between amino acids 39 and 40, *i.e.*, at the dash in the amino acid sequence ACT-CCA, based on the SignalP result. The predicted molecular weight of this protein is 16051.5 Daltons.

Table 4B. Encoded FCTR4 protein sequence (SEQ ID NO:15).

MNECMNEWTDNPQAKDLHDLPLPSFHFILTSTNTKSPSYVNTICTFMAPCFVICCSLCLEYKLSKYHPHFKIFSRKLPLSTPTLPP
PYRVSQSFLCATFVPVSTVALIKLHCVSHFLDCELFEAEDYLFISLPPMPRTGPS

The predicted amino acid sequence was searched in the publicly available GenBank database FCTR4 protein showed 30 % identities (22 over 72 amino acids) and 43% homologies (31over 72 amino acids) with hypothetical 10 kD protein of *Trypanosoma cruzi* (86 aa; ACC:Q99233) shown in Table 4C. The best homologies with a human protein were 54 % identities (114 over 343 amino acids) with NF-Kappa-B P65delta3 protein (71 aa fragment; ACC:Q13313) (SEQ ID NO:77).

Table 4C. BLASTP of FCTR4 against protein sequences

BLAST X search results are shown below:

ptnr:SPTREMBL-ACC:Q99233 HYPOTHETICAL 10 KD PROTEIN +3, 68, 0.60, 1, (SEQ ID

NO:73)

ptnr:SPTREMBL-ACC:[redacted]6896 GABA RECEPTOR SUBUNIT - AEDES +3, 66, 0.81, 4 (SEQ ID NO:74)

ptnr:SPTREMBL-ACC:O76473 GABA RECEPTOR SUBUNIT - LEPTI... +3, 66, 0.99, 2 (SEQ ID NO:75)

ptnr:TREMBLNEW-ACC:AAD28317 F13J11.13 PROTEIN - Arabid... +3, 62, 0.99, 1 (SEQ ID NO:76)

Based upon homology, FCTR4 proteins and each homologous protein or peptide may share at least some activity.

FCTR5

FCTR5 is a protein bearing sequence homology to human complement C1R component precursor. The clone is expressed in breast, heart, lung, fetal lung, salivary gland, adrenal gland, spleen, kidney, and fetal kidney.

The novel FCTR5 nucleic acid of 1667 nucleotides (also referred to as 32125243.0.21) is shown in Table 5A. An ORF begins with an ATG initiation codon at nucleotides 34-36 and ends with a TGA codon at nucleotides 1495-1497. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 5A, and the start and stop codons are in bold letters.

Table 5A. FCTR5a Nucleotide Sequence (SEQ ID NO:16)

GTTCTCTCGCAGGTCCCAGATGTCCAGTTCCAG**ATG**CCTGGACCCAGAGTGTGGGGGAAATATCTCTGGAGAAGCCCTCA
CTCCAAAGGCTGTCCAGGCGCAATGTGGTGGCTGCTTCTCTGGGGAGTCCTCCAGGCTTGCCCAACCCGGGGCTCCGTCC
TCTTGGCCCAAGAGCTACCCCAGCAGCTGACATCCCCCGGGTACCCAGAGCCGTATGGCAAAGGCCAAGAGAGCAGCACG
GACATCAAGGCTCCAGAGGGCTTTGCTGTGAGGCTCGTCTTCCAGGACTTCGACCTGGAGCCGTCCCAGGACTGTGCAGG
GGACTCTGTCACAATCTCATTCGTCGGTTCGGATCCAAGCCAGTTCTGTGGTCAGCAAGGCTCCCCTCTGGGCAGGCCCC
CTGGTCAGAGGGAGTTTGTATCCTCAGGGAGGAGTTTGCGGCTGACCTTCCGCACACAGCCTTCCTCGGAGAACAAGACT
GCCCACCTCCACAAGGGCTTCCTGGCCCTCTACCAAACCGTGGCTGTGAACTATAGTCAGCCCATCAGCGAGGCCAGCAG
GGGCTCTGAGGCCATCAACGCACCTGGAGACAACCCTGCCAAGGTCCAGAACCACTGCCAGGAGCCCTATTATCAGGCCG
CGGCAGCAGGGGCACTCACCTGTGCAACCCCAGGGACCTGGAAAGACAGACAGGATGGGGAGGAGGTTCTTCAGTGTATG
CCTGTCTGCGGACGGCCAGTCACCCCCATTGCCCAGAATCAGACGACCCTCGGTTCTTCCAGAGCCAAGCTGGGCAACTT
CCCCTGGCAAGCCTTCACCAGTATCCACGGCCGTGGGGGCGGGGCCCTGCTGGGGGACAGATGGATCCTCACTGCTGCCC
ACACCATCTACCCCAAGGACAGTGTTTCTCTCAGGAAGAACCAGAGTGTGAATGTGTTCTTGGGCCACACAGCCATAGAT
GAGATGCTGAAACTGGGGAACCACCCTGTCCACCGTGTCGTTGTGCACCCCGACTACCGTCAGAATGAGTCCCATAACTT
TAGCGGGGACATCGCCCTCCTGGAGCTGCAGCACAGCATCCCCCTGGGCCCCAACGTCCTCCCGGTCTGTCTGCCCGATA
ATGAGACCCTCTACCGCAGCGGCTTGTTGGGCTACGTCAGTGGGTTTGGCATGGAGATGGGCTGGCTAACTACTGAGCTG
AAGTACTCGAGGCTGCCTGTAGCTCCCAGGGAGGCCTGCAACGCCTGGCTCCAAAAGAGACAGAGACCCGAGGTGTTTTC
TGACAATATGTTCTGTGTTGGGGATGAGACGCAAAGGCACAGTGTCTGCCAGGGGGACAGTGGCAGCCTCTATGTGGTAT
GGGACAATCATGCCCATCACTGGGTGGCCACGGGCATTGTGTCCTGGGGCATAGGGTGTGGCGAAGGGTATGACTTCTAC
ACCAAGGTGCTCAGCTATGTGGACTGGATCAAGGGAGTGATGAATGGCAAGAATT**GA**CCCTGGGGGCTTGAACAGGGACT
GACCAGCACAGTGGAGGCCCCAGGCAACAGAGGGCCTGGAGTGAGGACTGAACACTGGGGTAGGGGGTGGGGGTTTCTCT
TGCAGTGGCTTGGTGCAACAGTGATGTGAATAGGATTTCCCTTTTTTTTTTTTTTTTTAAAAAAAAA

The FCTR5 protein encoded by SEQ ID NO:16 has 487 amino acid residues, and is presented using the one-letter code in Table 5B. FCTR5 was searched against other databases using SignalPep and PSort search protocols. The FCTR5 protein is most likely microbody (peroxisome) (Certainty=0.6406) and seems to have no N-terminal signal sequence. The predicted molecular weight of FCTR5 protein is 53511.9 daltons.

Table 5B. Encoded FCTR5a protein sequence (SEQ ID NO:17).

```
MPGPRVWGKYLWRSPHSKGCPGAMWWLLLWGVLQACPTRGSVLLAQELPQQLTSPGYPEPYGKGQESSTDIKAPEGFAVRLVFQDF
DLEPSQDCAGDSVTISFVGSDPSQFCGQQGSPLGRPPGQREFVSSGRSLRLTFRTQPSSENKTAHLHKGFLALYQTVAVNYSQPIS
EASRGSEAINAPGDNPAKVQNHCQEPYYQAAAAGALTCATPGTWKDRQDGEEVLQCMPVCGRPVTPIAQNQTTLGSSRAKLGNFPW
QAFTSIHGRGGGALLGDRWILTAAHTIYPKDSVSLRKNQSVNVFLGHTAIDEMLKLGNHPVHRVVVHPDYRQNESHNFSGDIALLE
LQHSIPLGPNVLPVCLPDNETLYRSGLLGYVSGFGMEMGWLTTELKYSRLPVAPREACNAWLQKRQRPEVFSDNMFCVGDETQRHS
VCQGDSGSLYVVWDNHAHHWVATGIVSWGIGCGEGYDFYTKVLSYVDWIKGVMNGKN
```

An alternative embodiment, FCTR5b, is a 1691 base sequence shown in Table 5C.

Table 5C. FCTR5b Nucleotide Sequence (SEQ ID NO:18)

```
TTTTTTTTTAAAAAAAAAAAAAAAAAGGGAAATCCTATTCACATCACTGTTGCACCAAGCCACTGCAAGAGAAACCCCCACCCCCT
ACCCCAGTGTTCAGTCCTCACTCCAGGCCCTCTGTTGCCTGGGGCCTCCACTGTGCTGGTCAGTCCCTGTTCAAGCCCCCAGGGTC
AATTCTTGCCATTCATCACTCCCTTGATCCAGTCCACATAGCTGAGCACCTTGGTGTAGAAGTCATACCCTTCGCCACACCCTATG
CCCCAGGACACAATGCCCGTGGCCACCCAGTGATGGGCATGATTGTCCCATACCACATAGAGGCTGCCACTGTCCCCCTGGCAGAC
ACTGTGCCTTTGCGTCTCATCCCCAACACAGAACATATTGTCAGAAAACACCTCGGGTCTCTGTCTCTTTTGGAGCCAGGCGTTGC
AGGCCTCCCTGGGAGCTACAGGCAGCCTCGAGTACTTCAGCTCAGTAGTTAGCCAGCCCATCTCCATGCCAAACCCACTGACGTAG
CCCAACAAGCCGCTGCGGTAGAGGGTCTCATTATCGGGCAGACAGACCGGGAGGACGTTGGGGCCCAGGGGGATGCTGTGCTGCAG
CTCCAGGAGGGCGATGTCCCCGCTAAAGTTATGGGACTCATTCTGACGGTAGTCGGGGTGCACAACGACACGGTGGACAGGGTGGT
TCCCCAGTTTCAGCATCTCATCTATGGCTGTGTGGCCCAAGAACACATTCACACTCTGGTTCTTCCTGAGAGAAACACTGTCCTTG
GGGTAGATGGTGTGGGCAGCAGTGAGGATCCATCTGTCCCCCAGCAGGGCCCCGCCCCCACGGCCGTGGATACTGGTGAAGGCTTG
CCAGGGGAAGTTGCCCAGCTTGGCTCTGGAAGAACCGAGGGTCGTCTGATTCTGGGCAATGGGGGTGACTGGCCGTCCGCAGACAG
GCATACACTGAAGAACCTCCTCCCCATCCTGTCTGTCTTTCCAGGTCCCTGGGGTTGCACAGGTGAGTGCCCCTGCTGCCGCGGCC
TGATAATAGGGCTCCTGGCAGTGGTTCTGGACCTTGGCAGGGTTGTCTCCAGGTGCGTTGATGGCCTCAGAGCCCCTGCTGGCCTC
GCTGATGGGCTGACTATAGTTCACAGCCACGGTTTGGTAGAGGGCCAGGAAGCCCTTGTGGAGGTGGGCAGTCTTGTTCTCCGAGG
AAGGCTGTGTGCGGAAGGTCAGCCGCAAACTCCTCCCTGAGGATACAAACTCCCTCTGACCAGGGGGCCTGCCCAGAGGGGAGCCT
TGCTGACCACAGAACTGGCTTGGATCCGAACCGACGAATGAGATTGTGACAGAGTCCCCTGCACAGTCCTGGGACGGCTCCAGGTC
GAAGTCCTGGAAGACGAGCCTCACAGCAAAGCCCTCTGGAGCCTTGATGTCCGTGCTGCTCTCTTGGCCTTTGCCATACGGCTCTG
GGTACCCGGGGGATGTCAGCTGCTGGGGTAGCTCTTGGGCCAAGAGGACGGAGCCCCGGGTTGGGCAAGCCTGGAGGACTCCCCAG
AGAAGCAGCCACCACATTGCGCCTGGACAGCCTTTGGAGTGAGGGCTTCTCCAGAGATATTTCCCCCACACTCTGGGTCCAGGCAT
CTGGAACTGGACATCTGGGACCTGCGAGAGAACTGGCCCAGGATAGGGAACAAAAGG
```

The FCTR5b protein encoded by SEQ ID NO:18 has 487 amino acid residues, and is presented using the one-letter code in Table 5D. FCTR5 was searched against other databases using SignalPep and PSort search protocols. The FCTR5b protein is most likely microbody (peroxisome) (Certainty=0.6406) and seems to have no N-terminal signal sequence. The predicted molecular weight of FCTR5 protein is 53511.9 daltons.

Table 5D. Encoded FCTR5b protein sequence (SEQ ID NO:19).

```
MPGPRVWGKYLWRSPHSKGCPGAMWWLLLWGVLQACPTRGSVLLAQQLPQQLTSPGYPEPYGKGQESSTDIKAPEGFAVRLVFQDF
DLEPSQDCAGDSVTISFVGSDPSQFCGQQGSPLGRPPGQREFVSSGRSLRLTFRTQPSSENKTAHLHKGFLALYQTVAVNYSQPIS
EASRGSEAINAPGDNPAKVQNHCQEPYYQAAAAGALTCATPGTWKDRQDGEEVLQCMPVCGRPVTPIAQNQTTLGSSRAKLGNFPW
QAFTSIHGRGGGALLGDRWILTAAHTIYPKDSVSLRKNQSVNVFLGHTAIDEMLKLGNHPVHRVVVHPDYRQNESHNFSGDIALLE
LQHSIPLGPNVLPVCLPDNETLYRSGLLGYVSGFGMEMGWLTTELKYSRLPVAPREACNAWLQKRQRPEVFSDNMFCVGDETQRHS
VCQGDSGSLYVVWDNHAHHWVATGIVSWGIGCGEGYDFYTKVLSYVDWIKGVMNGKN
```

The predicted amino acid sequence was searched in the publicly available GenBank database FCTR5a protein showed 58 % identities (177 over 302 amino acids) and 74 % homologies (226 over 302 amino acids) with human complement C1R component precursor (EC 3.4.21.41) (705 aa.; ACC:P00736). Based upon homology, FCTR5 proteins and each homologous protein or peptide may share at least some activity.

In a search of sequence databases, it was found, for example, that the nucleic acid sequence the nucleotides 17-1594 of FCTR5a have 1575 of 1578 bases (99 %) identical to *Homo sapiens* complement C1r-like proteinase precursor (GENBANK-ID: XM_007061.1) (SEQ ID NO:78) (Table 5E).

Table 5E. BLASTN of FCTR5a against *Homo sapiens* complement C1r-like proteinase precursor (SEQ ID NO:78)

```
>GI|11436767|REF|XM_007061.1| HOMO SAPIENS COMPLEMENT C1R-LIKE PROTEINASE PRECURSOR,
(LOC51279),
            MRNA
          LENGTH = 3318

 SCORE = 3104 BITS (1566), EXPECT = 0.0
 IDENTITIES = 1575/1578 (99%)
 STRAND = PLUS / PLUS

QUERY: 17   CAGATGTCCAGTTCCAGATGCCTGGACCCAGAGTGTGGGGGAAATATCTCTGGAGAAGCC 76
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1    CAGATGTCCAGTTCCAGATGCCTGGACCCAGAGTGTGGGGGAAATATCTCTGGAGAAGCC 60

QUERY: 77   CTCACTCCAAAGGCTGTCCAGGCGCAATGTGGTGGCTGCTTCTCTGGGGAGTCCTCCAGG 136
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 61   CTCACTCCAAAGGCTGTCCAGGCGCAATGTGGTGGCTGCTTCTCTGGGGAGTCCTCCAGG 120

QUERY: 137  CTTGCCCAACCCGGGGCTCCGTCCTCTTGGCCCAAGAGCTACCCCAGCAGCTGACATCCC 196
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 121  CTTGCCCAACCCGGGGCTCCGTCCTCTTGGCCCAAGAGCTACCCCAGCAGCTGACATCCC 180

QUERY: 197  CCGGGTACCCAGAGCCGTATGGCAAAGGCCAAGAGAGCAGCACGGACATCAAGGCTCCAG 256
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 181  CCGGGTACCCAGAGCCGTATGGCAAAGGCCAAGAGAGCAGCACGGACATCAAGGCTCCAG 240

QUERY: 257  AGGGCTTTGCTGTGAGGCTCGTCTTCCAGGACTTCGACCTGGAGCCGTCCCAGGACTGTG 316
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 241  AGGGCTTTGCTGTGAGGCTCGTCTTCCAGGACTTCGACCTGGAGCCGTCCCAGGACTGTG 300

QUERY: 317  CAGGGGACTCTGTCACAATCTCATTCGTCGGTTCGGATCCAAGCCAGTTCTGTGGTCAGC 376
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 301  CAGGGGACTCTGTCACAATCTCATTCGTCGGTTCGGATCCAAGCCAGTTCTGTGGTCAGC 360

QUERY: 377  AAGGCTCCCCTCTGGGCAGGCCCCCTGGTCAGAGGGAGTTTGTATCCTCAGGGAGGAGTT 436
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 361  AAGGCTCCCCTCTGGGCAGGCCCCCTGGTCAGAGGGAGTTTGTATCCTCAGGGAGGAGTT 420

QUERY: 437  TGCGGCTGACCTTCCGCACACAGCCTTCCTCGGAGAACAAGACTGCCCACCTCCACAAGG 496
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 421  TGCGGCTGACCTTCCGCACACAGCCTTCCTCGGAGAACAAGACTGCCCACCTCCACAAGG 480

QUERY: 497  GCTTCCTGGCCCTCTACCAAACCGTGGCTGTGAACTATAGTCAGCCCATCAGCGAGGCCA 556
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 481  GCTTCCTGGCCCTCTACCAAACCGTGGCTGTGAACTATAGTCAGCCCATCAGCGAGGCCA 540

QUERY: 557  GCAGGGGCTCTGAGGCCATCAACGCACCTGGAGACAACCCTGCCAAGGTCCAGAACCACT 616
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
```

```
SBJCT: 541  GCAGGGGCTCTGAGGCCATCAACGCACCTGGAGACAACCCTGCCAAGGTCCAGAACCACT 600

QUERY: 617  GCCAGGAG[redacted]ATTATCAGGCCGCGGCAGCAGGGGCACTCACCT[redacted]CAACCCCAGGGA 676
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 601  GCCAGGAGCCCTATTATCAGGCCGCGGCAGCAGGGGCACTCACCTGTGCAACCCCAGGGA 660

QUERY: 677  CCTGGAAAGACAGACAGGATGGGGAGGAGGTTCTTCAGTGTATGCCTGTCTGCGGACGGC 736
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 661  CCTGGAAAGACAGACAGGATGGGGAGGAGGTTCTTCAGTGTATGCCTGTCTGCGGACGGC 720

QUERY: 737  CAGTCACCCCCATTGCCCAGAATCAGACGACCCTCGGTTCTTCCAGAGCCAAGCTGGGCA 796
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 721  CAGTCACCCCCATTGCCCAGAATCAGACGACCCTCGGTTCTTCCAGAGCCAAGCTGGGCA 780

QUERY: 797  ACTTCCCCTGGCAAGCCTTCACCAGTATCCACGGCCGTGGGGGCGGGGCCCTGCTGGGGG 856
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 781  ACTTCCCCTGGCAAGCCTTCACCAGTATCCACGGCCGTGGGGGCGGGGCCCTGCTGGGGG 840

QUERY: 857  ACAGATGGATCCTCACTGCTGCCCACACCATCTACCCCAAGGACAGTGTTTCTCTCAGGA 916
            |||||||||||||||||||||||||||| ||||||||||||||||||||||||||||||
SBJCT: 841  ACAGATGGATCCTCACTGCTGCCCACACCGTCTACCCCAAGGACAGTGTTTCTCTCAGGA 900

QUERY: 917  AGAACCAGAGTGTGAATGTGTTCTTGGGCCACACAGCCATAGATGAGATGCTGAAACTGG 976
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 901  AGAACCAGAGTGTGAATGTGTTCTTGGGCCACACAGCCATAGATGAGATGCTGAAACTGG 960

QUERY: 977  GGAACCACCCTGTCCACCGTGTCGTTGTGCACCCCGACTACCGTCAGAATGAGTCCCATA 1036
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 961  GGAACCACCCTGTCCACCGTGTCGTTGTGCACCCCGACTACCGTCAGAATGAGTCCCATA 1020

QUERY: 1037 ACTTTAGCGGGGACATCGCCCTCCTGGAGCTGCAGCACAGCATCCCCCTGGGCCCCAACG 1096
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1021 ACTTTAGCGGGGACATCGCCCTCCTGGAGCTGCAGCACAGCATCCCCCTGGGCCCCAACG 1080

QUERY: 1097 TCCTCCCGGTCTGTCTGCCCGATAATGAGACCCTCTACCGCAGCGGCTTGTTGGGCTACG 1156
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1081 TCCTCCCGGTCTGTCTGCCCGATAATGAGACCCTCTACCGCAGCGGCTTGTTGGGCTACG 1140

QUERY: 1157 TCAGTGGGTTTGGCATGGAGATGGGCTGGCTAACTACTGAGCTGAAGTACTCGAGGCTGC 1216
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1141 TCAGTGGGTTTGGCATGGAGATGGGCTGGCTAACTACTGAGCTGAAGTACTCGAGGCTGC 1200

QUERY: 1217 CTGTAGCTCCCAGGGAGGCCTGCAACGCCTGGCTCCAAAAGAGACAGAGACCCGAGGTGT 1276
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1201 CTGTAGCTCCCAGGGAGGCCTGCAACGCCTGGCTCCAAAAGAGACAGAGACCCGAGGTGT 1260

QUERY: 1277 TTTCTGACAATATGTTCTGTGTTGGGGATGAGACGCAAAGGCACAGTGTCTGCCAGGGGG 1336
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1261 TTTCTGACAATATGTTCTGTGTTGGGGATGAGACGCAAAGGCACAGTGTCTGCCAGGGGG 1320

QUERY: 1337 ACAGTGGCAGCCTCTATGTGGTATGGGACAATCATGCCCATCACTGGGTGGCCACGGGCA 1396
            |||||||||||| ||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1321 ACAGTGGCAGCGTCTATGTGGTATGGGACAATCATGCCCATCACTGGGTGGCCACGGGCA 1380

QUERY: 1397 TTGTGTCCTGGGGCATAGGGTGTGGCGAAGGGTATGACTTCTACACCAAGGTGCTCAGCT 1456
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1381 TTGTGTCCTGGGGCATAGGGTGTGGCGAAGGGTATGACTTCTACACCAAGGTGCTCAGCT 1440

QUERY: 1457 ATGTGGACTGGATCAAGGGAGTGATGAATGGCAAGAATTGACCCTGGGGGCTTGAACAGG 1516
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1441 ATGTGGACTGGATCAAGGGAGTGATGAATGGCAAGAATTGACCCTGGGGGCTTGAACAGG 1500

QUERY: 1517 GACTGACCAGCACAGTGGAGGCCCCAGGCAACAGAGGGCCTGGAGTGAGGACTGAACACT 1576
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1501 GACTGACCAGCACAGTGGAGGCCCCAGGCAACAGAGGGCCTGGAGTGAGGACTGAACACT 1560

QUERY: 1577 GGGGTAGGGGGTGGGGGT 1594
            |||||||||| |||||||
SBJCT: 1561 GGGGTAGGGGTTGGGGGT 1578
```

In this search it was also found that the FCTR5a nucleic acid had homology to three fragments of *Homo sapiens* complement component 1, r subcomponent. It has 102 of 117 bases (87%) identical to 1458-1574, 82 of 94 bases (87%) identical to 2052-2145, and 54 of 63 bases (85%) identical to 1678-1740 all fragments of *Homo sapiens* complement component 1, r subcomponent (GenBank Acc: NM_001733.1) (Table 5F).

Table 5F. BLASTN of FCTR5a against *Homo sapiens* complement component 1, r subcomponent (SEQ ID NO:79)

```
>GI|4502492|REF|NM_001733.1| HOMO SAPIENS COMPLEMENT COMPONENT 1, R SUBCOMPONENT
(C1R), MRNA
          LENGTH = 2386

 SCORE =  113 BITS (57), EXPECT = 3E-22
 IDENTITIES = 102/117 (87%)
 STRAND = PLUS / PLUS

QUERY: 783  AGCCAAGCTGGGCAACTTCCCCTGGCAAGCCTTCACCAGTATCCACGGCCGTGGGGGCGG 842
            ||||||| |||||||||||||||||||| |  |||||||  |||||||| || ||||||||
SBJCT: 1458 AGCCAAGATGGGCAACTTCCCCTGGCAGGTGTTCACCAACATCCACGGGCGCGGGGGCGG 1517

QUERY: 843  GGCCCTGCTGGGGGACAGATGGATCCTCACTGCTGCCCACACCATCTACCCCAAGGA 899
            |||||||||||| ||| | |||||||||||| |||||||||||| | || ||||||||
SBJCT: 1518 GGCCCTGCTGGGCGACCGCTGGATCCTCACAGCTGCCCACACCCTGTATCCCAAGGA 1574


SCORE = 91.7 BITS (46), EXPECT = 1E-15
 IDENTITIES = 82/94 (87%)
 STRAND = PLUS / PLUS

QUERY: 1380 CTGGGTGGCCACGGGCATTGTGTCCTGGGGCATAGGGTGTGGCGAAGGGTATGACTTCTA 1439
            |||||||||||||||||| |||||||||||||| |||||  ||   || |||| ||||||
SBJCT: 2052 CTGGGTGGCCACGGGCATCGTGTCCTGGGGCATCGGGTGCAGCAGGGGCTATGGCTTCTA 2111

QUERY: 1440 CACCAAGGTGCTCAGCTATGTGGACTGGATCAAG 1473
            |||||| ||||||| ||| ||||||||||||||||
SBJCT: 2112 CACCAAAGTGCTCAACTACGTGGACTGGATCAAG 2145


SCORE = 54.0 BITS (27), EXPECT = 2E-04
 IDENTITIES = 54/63 (85%)
 STRAND = PLUS / PLUS

QUERY: 1006 CACCCCGACTACCGTCAGAATGAGTCCCATAACTTTAGCGGGGACATCGCCCTCCTGGAG 1065
            ||||| |||||||||||| |||||||| | || |||   |||||||||||||| ||||||
SBJCT: 1678 CACCCGGACTACCGTCAGGATGAGTCCTACAATTTTGAGGGGGACATCGCCCTGCTGGAG 1737

QUERY: 1066 CTG 1068
            |||
SBJCT: 1738 CTG 1740
```

The amino acid sequence of the protein of FCTR5a 485 of 487 amino acid residues (99%) identical to, and 487 of 487 residues (100%) positive with, the 487 amino acid complement C1r-like proteinase precursor from *Homo sapiens* (GenBank-ACC: AAF44349.1) (SEQ ID NO:80) (Table 5G).

Table 5G. BLASTP of FCTR5a and b against Complement C1R-like proteinase precursor (SEQ ID NO:80)

```
>GI|7706083|REF|NP_057630.1| COMPLEMENT C1R-LIKE PROTEINASE PRECURSOR, [HOMO SAPIENS]
 GI|11436768|REF|XP_007061.1| COMPLEMENT C1R-LIKE PROTEINASE PRECURSOR, [HOMO SAPIENS]
 GI|7271475|GB|AAF44349.1|AF178985_1 (AF178985) COMPLEMENT C1R-LIKE PROTEINASE
PRECURSOR [HOMO SAPIENS]
          LENGTH = 487

 SCORE =  972 BITS (2513), EXPECT = 0.0
 IDENTITIES = 485/487 (99%), POSITIVES = 487/487 (100%)
                                                                    R
QUERY: 1   MPGPRVWGKYLWRSPHSKGCPGAMWWLLLWGVLQACPTRGSVLLAQELPQQLTSPGYPEP 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1   MPGPRVWGKYLWRSPHSKGCPGAMWWLLLWGVLQACPTRGSVLLAQELPQQLTSPGYPEP 60

QUERY: 61  YGKGQESSTDIKAPEGFAVRLVFQDFDLEPSQDCAGDSVTISFVGSDPSQFCGQQGSPLG 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 61  YGKGQESSTDIKAPEGFAVRLVFQDFDLEPSQDCAGDSVTISFVGSDPSQFCGQQGSPLG 120

QUERY: 121 RPPGQREFVSSGRSLRLTFRTQPSSENKTAHLHKGFLALYQTVAVNYSQPISEASRGSEA 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 121 RPPGQREFVSSGRSLRLTFRTQPSSENKTAHLHKGFLALYQTVAVNYSQPISEASRGSEA 180

QUERY: 181 INAPGDNPAKVQNHCQEPYYQAAAAGALTCATPGTWKDRQDGEEVLQCMPVCGRPVTPIA 240
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 181 INAPGDNPAKVQNHCQEPYYQAAAAGALTCATPGTWKDRQDGEEVLQCMPVCGRPVTPIA 240

QUERY: 241 QNQTTLGSSRAKLGNFPWQAFTSIHGRGGGALLGDRWILTAAHTIYPKDSVSLRKNQSVN 300
           ||||||||||||||||||||||||||||||||||||||||+|||||||||||||||||||
SBJCT: 241 QNQTTLGSSRAKLGNFPWQAFTSIHGRGGGALLGDRWILTAAHTVYPKDSVSLRKNQSVN 300

QUERY: 301 VFLGHTAIDEMLKLGNHPVHRVVVHPDYRQNESHNFSGDIALLELQHSIPLGPNVLPVCL 360
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 301 VFLGHTAIDEMLKLGNHPVHRVVVHPDYRQNESHNFSGDIALLELQHSIPLGPNVLPVCL 360

QUERY: 361 PDNETLYRSGLLGYVSGFGMEMGWLTTELKYSRLPVAPREACNAWLQKRQRPEVFSDNMF 420
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 361 PDNETLYRSGLLGYVSGFGMEMGWLTTELKYSRLPVAPREACNAWLQKRQRPEVFSDNMF 420

QUERY: 421 CVGDETQRHSVCQGDSGSLYVVWDNHAHHWVATGIVSWGIGCGEGYDFYTKVLSYVDWIK 480
           ||||||||||||||||+||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 421 CVGDETQRHSVCQGDSGSVYVVWDNHAHHWVATGIVSWGIGCGEGYDFYTKVLSYVDWIK 480

QUERY: 481 GVMNGKN 487
           |||||||
SBJCT: 481 GVMNGKN 487

R = AT RESIDUE 46, FCTR5B DIFFERS FROM FCTR5A IN THAT Q46R. THE REST OF THE HOMOLOGY
IS THE SAME.
```

The full amino acid sequence of the protein of FCTR5a has 175 of 303 amino acid residues (58%) identical to, and 226 of 303 residues (74%) positive with the 400-701 amino acid segment, 72 of 157 residues (45%) identical and 94 of 157 residues (59%) positive with amino acids 1-155, and 36 of 139 residues (25%) identical and 58 of 139 residues (40%) positive with amino acids 188-312 of the 705 amino acid Complement C1R Component Precursor from *Homo sapiens* (GenBank-ACC: AAA51851.1) (SEQ ID NO:43) (Table 5H).

Table 5H. BLASTP of FCTR5a and b against Complement C1R Component Precursor (SEQ ID NO:81)

```
>GI|115204|SP|P00736|C1R_HUMAN COMPLEMENT C1R COMPONENT PRECURSOR
 GI|67614|PIR||C1HURB COMPLEMENT SUBCOMPONENT C1R (EC 3.4.21.41) PRECURSOR - HUMAN
 GI|179644|GB|AAA51851.1| (M14058) HUMAN COMPLEMENT C1R [HOMO SAPIENS]
          LENGTH = 705

 SCORE =  361 BITS (928), EXPECT = 8E-99
 IDENTITIES = 175/303 (58%), POSITIVES = 226/303 (74%), GAPS = 9/303 (2%)

QUERY: 189 AKVQNHCQEPYYQ--------AAAAGALTCATPGTWKDRQDGEEVLQCMPVCGRPVTPIA 240
           |++| +| ||||+            |  ||   | ||+ | ||++ +|+||||+|| |+
SBJCT: 400 ARIQYYCHEPYYKMQTRAGSRESEQGVYTCTAQGIWKNEQKGEKIPRCLPVCGKPVNPVE 459

QUERY: 241 QNQTTLGSSRAKLGNFPWQAFTSIHGRGGGALLGDRWILTAAHTIYPKDSVSLRKNQSVN 300
           | |  +|  +||+|||||| ||+|||||||||||||||||||||+|||+  + + | |++
SBJCT: 460 QRQRIIGGQKAKMGNFPWQVFTNIHGRGGGALLGDRWILTAAHTLYPKEHEA-QSNASLD 518

QUERY: 301 VFLGHTAIDEMLKLGNHPVHRVVVHPDYRQNESHNFSGDIALLELQHSIPLGPNVLPVCL 360
           |||||| ++|++|||||||+ || |||||||+||+|| ||||||||++|+ ||||+||+||
SBJCT: 519 VFLGHTNVEELMKLGNHPIRRVSVHPDYRQDESYNFEGDIALLELENSVTLGPNLLPICL 578

QUERY: 361 PDNETLYRSGLLGYVSGFGMEMGWLTTELKYSRLPVAPREACNAWLQKRQRPEVFSDNMF 420
           |||+| |  ||+|||||||+    +  +|++ |||||  +||  ||+ + | +||| |||
SBJCT: 579 PDNDTFYDLGLMGYVSGFGVMEEKIAHDLRFVRLPVANPQACENWLRGKNRMDVFSQNMF 638

QUERY: 421 CVGDETQRHSVCQGDSGSLYVVWDNHAHHWVATGIVSWGIGCGEGYDFYTKVLSYVDWIK 480
           | |  + +   |||||| ++ | | +   |||||||||||||  || ||||||+||||||
SBJCT: 639 CAGHPSLKQDACQGDSGGVFAVRDPNTDRWVATGIVSWGIGCSRGYGFYTKVLNYVDWIK 698

QUERY: 481 GVM 483
             |
SBJCT: 699 KEM 701


 SCORE =  122 BITS (306), EXPECT = 1E-26
 IDENTITIES = 72/157 (45%), POSITIVES = 94/157 (59%), GAPS = 3/157 (1%)
                                  R
QUERY: 24  MWWLLLWGVLQACPTRGSVLLAQELPQQLTSPGYPEPYGKGQESSTDIKAPEGFAVRLVF 83
           || | |       |   ||+ + |+|  ++||| +|+||    |++| |  | |+ |+|||
SBJCT: 1   MWLLYLLVPALFCRAGGSIPIPQKLFGEVTSPLFPKPYPNNFETTTVITVPTGYRVKLVF 60

QUERY: 84  QDFDLEPSQDCAGDSVTISFVGSDPSQFCGQQGSPLGRPPGQREFVSSGRSLRLTFRTQP 143
           | |||||+ |  | | ||       +|||| ||||| |||++||+| |  + ||| |
SBJCT: 61  QQFDLEPSEGCFYDYVKISADKKSLGRFCGQLGSPLGNPPGKKEFMSQGNKMLLTFHTDF 120

QUERY: 144 SS-ENKTAHLHKGFLALYQTVAVNYSQPISEASRGSE 179
           |+ || |   +|||||  ||  ||+  +  | +  | |
SBJCT: 121 SNEENGTIMFYKGFLAYYQ--AVDLDECASRSKSGEE 155


 SCORE = 36.3 BITS (83), EXPECT = 0.93
 IDENTITIES = 36/139 (25%), POSITIVES = 58/139 (40%), GAPS = 17/139 (12%)
                    R
QUERY: 35  ACPTRGSVLLAQELPQQLTSPGYPEPYGKGQESSTDIKAPEGFAVRLVF-QDFDLEPSQD 93
           +|    |  |  |    ++|  ||  |      +  |+   |  + | | + ||++  |
SBJCT: 188 SCQAECSSELYTEASGYISSLEYPRSYPPDLRCNYSIRVERGLTLHLKFLEPFDIDDHQQ 247

QUERY: 94  --CAGDSVTISFVGSDPSQFCGQQGSPLGRPPGQREFVSSGRSLRLTFRTQPSSENKTAH 151
             | | + |   | +  +|||+|     |||   +  +|  ++ | | |  | ++
SBJCT: 248 VHCPYDQLQIYANGKNIGEFCGKQ-----RPP---DLDTSSNAVDLLFFTDESGDS---- 295

QUERY: 152 LHKGFLALYQTVAVNYSQP 170
             +|+   | |  +   ||
SBJCT: 296 --RGWKLRYTTEIIKCPQP 312
```

R = AT RESIDUE 46, FCTR5B DIFFERS FROM FCTR5A IN THAT Q46R. THE REST OF THE HOMOLOGY IS THE SAME.

Based upon homology, FCTR5 proteins and each homologous protein or peptide may share at least some activity.

FCTR6

The novel nucleic acid of 1078 nucleotides FCTR6a (also designated 27455183.0.19) encoding a novel human blood coagulation factor XI-like protein is shown in Table 6A. An ORF was identified beginning with an ATG initiation codon at nucleotides 243-245 and ending with a TAA codon at nucleotides 1044-1046. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 6A, and the start and stop codons are in bold letters.

Table 6A FCTR6a Nucleotide Sequence (SEQ ID NO:20)

TTGATCCGTGCCAAGTGGCTTTTTGTGGGCTCTGTAGAGTGCTCTAAACCCAGCTCGGCCTTTGCTGTATTAGACAGAAGCACCTC
ATTCATATCCCTGGGGCCCCTGATGGTGCAGTGGTCTGGCTGTGGTCTGCACACCAGCTATTCTGTTTTGTTTTGTTTTGTTTTTT
TCCTACCTTTTTCCAATCCTCACACCTTCTGATCAACAGCCCCAGTAGGGTTTAAAGGTCCTAGAGCTAC**ATG**GGATTTAGGTTTC
TGGGCACAGCCAATTCTGCCACTTTTGAGACTTCCCTTCCCCTTCCACTTGCCCCTCTCTGGTTCTCTGCCACCAGTCCAGAAGAA
CTGAGTGTCGTGCTGGGGACCAACGACTTAACTAGCCCATCCATGGAAATAAAGGAGGTCGCCAGCATCATTCTTCACAAAGACTT
TAAGAGAGCCAACATGGACAATGACATTGCCTTGCTGCTGCTGGCTTCGCCCATCAAGCTCGATGACCTGAAGGTGCCCATCTGCC
TCCCCACGCAGCCCGGCCCTGCCACATGGCGCGAATGCTGGGTGGCAGGTTGGGGCCAGACCAATGCTGCTGACAAAAACTCTGTG
AAAACGGATCTGATGAAAGTGCCAATGGTCATCATGGACTGGGAGGAGTGTTCAAAGATGTTTCCAAAACTTACCAAAAATATGCT
GTGTGCCGGATACAAGAATGAGAGCTATGATGCCTGCAAGGGTGACAGTGGGGGGCCTCTGGTCTGCACCCCAGAGCCTGGTGAGA
AGTGGTACCAGGTGGGCATCATCAGCTGGGGAAAGAGCTGTGGAGATAAGAACACCCCAGGGATATACACCTCGTTGGTGAACTAC
AACCTCTGGATCGAGAAAGTGACCCAGCTAGGAGGCAGGCCCTTCAATGCAGAGAAAAGGAGGACTTCTGTCAAACAGAAACCTAT
GGGCTCCCCAGTCTCGGGAGTCCCAGAGCCAGGCAGCCCCAGATCCTGGCTCCTGCTCTGTCCCCTGTCCCATGTGTTGTTCAGAG
CTATTTTGTAC**TGA**TAATAAAATAGAGGCTATTCTTTCAACCGAAA

The FCTR6a protein encoded by SEQ ID NO:20 has 267 amino acid residues and is presented using the one-letter code in Table 6B. FCTR6a was searched against other databases using SignalPep and PSort search protocols. The FCTR6a protein is most likely mitochondrial matrix space (Certainty= 0.4372) and seems to have no N-terminal signal sequence. The predicted molecular weight of FCTR6a protein is 29412.8 daltons.

Table 6B. Encoded FCTR6a protein sequence (SEQ ID NO:21).

MGFRFLGTANSATFETSLPLPLAPLWFSATSPEELSVVLGTNDLTSPSMEIKEVASIILHKDFKRANMDNDIALLLLASPIKLDDL
KVPICLPTQPGPATWRECWVAGWGQTNAADKNSVKTDLMKVPMVIMDWEECSKMFPKLTKNMLCAGYKNESYDACKGDSGGPLVCT
PEPGEKWYQVGIISWGKSCGDKNTPGIYTSLVNYNLWIEKVTQLGGRPFNAEKRRTSVKQKPMGSPVSGVPEPGSPRSWLLLCPLS
HVLFRAILY

In an alternative embodiment, FCTR6b (alternatively referred to as 27455183.0.145) has the 1334 residue sequence shown in Table 6C. An ORF was identified beginning with an ATG initiation codon at nucleotides 499-501 and ending with a TAA codon at nucleotides 1300-1302. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 6C, and the start and stop codons are in bold letters.

Table 6C FCTR6b Nucleotide Sequence (SEQ ID NO:22)

GATTTTAGAAGGTTAATCAAA[redacted]CCGGGGACAGTTTCTTCATGGCATAACCACAGAC[redacted]TTGTGGCACCCGCTGT
CGTGGGATATCAAATATCCTCTGGGGTTCGGAATGTGGGCTTATTACTGAAGATCCTGTCTGCTTGGTCAGTGGCAGGTC
TAGACTAACTTCTGGTCCTGAGTTTCTAAAGTGCTGGTAGACCAGTTGATACAAAACAGATATAATAATGAATGCCTTAT
CTATCTGAAGGTCAGTTTGATCCGTGCCAAGTGGCTTTTTGTGGGCTGTGTAGAGTGCTCTAAACCCAGCTCGGCCTTTG
CTGTATTAGACAGAAGCACCTCATTCATATCCCTGGGGCCCCTGATGGTGCAGTGGTCTGGCTGTGGTCTGCACACCAGC
TATTCTGTTTTGTTTTGTTTTGTTTTGTTTTTTCCTACCTTTTTCCAATCCTCACACCTTCTGATCAACAGCCCCAGTAG
GGTTTAAAGGTCCTAGAGCTAC**ATG**GGATTTAGGTTTCTGGGCACAGCCAATTCTGCCACTTTTGAGACTTCCCTTCCCC
TTCCACTTGCCCCTCTCTGGTTCTCTGCCACCAGTCCAGAAGAACTGAGTGTCGTGCTGGGGACCAACGACTTAACTAGC
CCATCCATGGAAATAAAGGAGGTCGCCAGCATCATTCTTCACAAAGACTTTAAGAGAGCCAACATGGACAATGACATTGC
CTTGCTGCTGCTGGCTTCGCCCATCAAGCTCGATGACCTGAAGGTGCCCATCTGCCTCCCCACGCAGCCCGGCCCTGCCA
CATGGCGCGAATGCTGGGTGGCAGGTTGGGGCCAGACCAATGCTGCTGACAAAAACTCTGTGAAAACGGATCTGATGAAA
GTGCCAATGGTCATCATGGACTGGGAGGAGTGTTCAAAGATGTTTCCAAAACTTACCAAAAATATGCTGTGTGCCGGATA
CAAGAATGAGAGCTATGATGCCTGCAAGGGTGACAGTGGGGGGCCTCTGGTCTGCACCCCAGAGCCTGGTGAGAAGTGGT
ACCAGGTGGGCATCATCAGCTGGGGAAAGAGCTGTGGAGAGAAGAACACCCCAGGGATATACACCTCGTTGGTGAACTAC
AACCTCTGGATCGAGAAAGTGACCCAGCTAGAGGGCAGGCCCTTCAATGCAGAGAAAAGGAGGACTTCTGTCAAACAGAA
ACCTATGGGCTCCCCAGTCTCGGGAGTCCCAGAGCCAGGCAGCCCCAGATCCTGGCTCCTGCTCTGTCCCCTGTCCCATG
TGTTGTTCAGAGCTATTTTGTAC**TGA**TAATAAAATAGAGGCTATTCTTTCAACCGAAA

The FCTR6b protein encoded by SEQ ID NO:22 has 267 amino acid residues and is presented using the one-letter code in Table 6B. The Psort profile for FCTR4 predicts that this sequence has no N-terminal signal peptide and is likely to be localized at the mitochondrial matrix space (Certainty=0.4372). The predicted molecular weight of this protein is 29498.9 Daltons.

Table 6D. Encoded FCTR6b protein sequence (SEQ ID NO:23).

MGFRFLGTANSATFETSLPLPLAPLWFSATSPEELSVVLGTNDLTSPSMEIKEVASIILHKDFKRANMDNDIALLLLASPIKLDDL
KVPICLPTQPGPATWRECWVAGWGQTNAADKNSVKTDLMKVPMVIMDWEECSKMFPKLTKNMLCAGYKNESYDACKGDSGGPLVCT
PEPGEKWYQVGIISWGKSCGEKNTPGIYTSLVNYNLWIEKVTQLEGRPFNAEKRRTSVKQKPMGSPVSGVPEPGSPRSWLLLCPLS
HVLFRAILY

In a search of sequence databases, it was found, for example, that the FCTR6a nucleic acid sequence has 853 of 897 bases (95 %) identical to bases 551-1447, and 346 of 388 bases (89%) identical to bases 127-513 of *Macaca fascicularis* brain cDNA, clone QccE-17034 (GENBANK-ID: |AB046651) (Table 6E).

Table 6E. BLASTN of FCTR6a against *Macaca fascicularis* brain cDNA, clone QccE-17034 (SEQ ID NO:82)

```
>GI|9651112|DBJ|AB046651.1|AB046651 MACACA FASCICULARIS BRAIN CDNA, CLONE QCCE-17034
          LENGTH = 1746

 SCORE = 1429 BITS (721), EXPECT = 0.0
 IDENTITIES = 853/897 (95%)
 STRAND = PLUS / PLUS

QUERY: 434  CCTTTTTCCAATCCTCACACCTTCTGATCAACAGCCCCAGTAGGGTTTAAAGGTCCTAGA 493
            |||||||||||||||||||||||||| | ||||||||||||||| |||| ||||||||
SBJCT: 551  CCTTTTTCCAATCCTCACACCTTCTGAGCTACAGCCCCAGTAGGGTCTAAATGTCCTAGA 610

QUERY: 494  GCTACATGGGATTTAGGTTTCTGGGCACAGCCAATTCTGCCACTTTTGAGACTTCCCTTC 553
            |||| ||| |||||||||||||| |||||||||||||| |||||||||| |||||||||
SBJCT: 611  GCTATATGAGATTTAGGTTTCTGAGCACAGCCAATTCTCCCACTTTTGAGGCTTCCCTTC 670

QUERY: 554  CCCTTCCACTTGCCCCTCTCTGGTTCTCTGCCACCAGTCCAGAAGAACTGAGTGTCGTGC 613
            ||||| |||| |||||||||||||||||||||||||||||||||||||||||| ||||||||
```

```
SBJCT: 671  CCCTTTCACTCGCCCCTCTCTGGTTCTCTGCCACCAGTCCAGAAGA TGAATGTCGTGC 730

QUERY: 614  TGGGGACCA ACTTAACTAGCCCATCCATGGAAATAAAGGAGGT CCAGCATCATTC 673
            |||||||||||||||||||||||| ||||||||||||||||||||||||||||||||||
SBJCT: 731  TGGGGACCAACGACTTAACTAGCTCATCCATGGAAATAAAGGAGGTCGCCAGCATCATTC 790

QUERY: 674  TTCACAAAGACTTTAAGAGAGCCAACATGGACAATGACATTGCCTTGCTGCTGCTGGCTT 733
            ||||||| |||||||||||||||||||||||||||||||||||||||||||||||||| |
SBJCT: 791  TTCACAAGGACTTTAAGAGAGCCAACATGGACAATGACATTGCCTTGCTGCTGCTGGCCT 850

QUERY: 734  CGCCCATCAAGCTCGATGACCTGAAGGTGCCCATCTGCCTCCCCACGCAGCCCGGCCCTG 793
            ||||||||| |||||||||||||||||||||||||||||| ||||||| |||||| |
SBJCT: 851  CGCCCATCACACTCGATGACCTGAAGGTGCCCATCTGCCTCCCTACGCAGCACGGCCCCG 910

QUERY: 794  CCACATGGCGCGAATGCTGGGTGGCAGGTTGGGGCCAGACCAATGCTGCTGACAAAAACT 853
            ||||||||| ||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 911  CCACATGGCACGAATGCTGGGTGGCAGGTTGGGGCCAGACCAATGCTGCTGACAAAAACT 970

QUERY: 854  CTGTGAAAACGGATCTGATGAAAGTGCCAATGGTCATCATGGACTGGGAGGAGTGTTCAA 913
            |||||||||||||||||||||||| ||| ||||||||||||||||||||||||||||||
SBJCT: 971  CTGTGAAAACGGATCTGATGAAAGCGCCGATGGTCATCATGGACTGGGAGGAGTGTTCAA 1030

QUERY: 914  AGATGTTTCCAAAACTTACCAAAAATATGCTGTGTGCCGGATACAAGAATGAGAGCTATG 973
            ||  |||||||||||| |||||||||||||||||||| |||||||| ||||||||||||
SBJCT: 1031 AGGCGTTTCCAAAACTCACCAAAAATATGCTGTGTGCTGGATACAATAATGAGAGCTATG 1090

QUERY: 974  ATGCCTGCAAGGGTGACAGTGGGGGGCCTCTGGTCTGCACCCCAGAGCCTGGTGAGAAGT 1033
            | |||||| |||||||||| ||||| ||||||||||||||||||||||||||||||||||
SBJCT: 1091 ACGCCTGCCAGGGTGACAGCGGGGGACCTCTGGTCTGCACCCCAGAGCCTGGTGAGAAGT 1150

QUERY: 1034 GGTACCAGGTGGGCATCATCAGCTGGGGAAAGAGCTGTGGAGAGAAGAACACCCCAGGGA 1093
            |||||||||||||| ||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1151 GGTACCAGGTGGGTATCATCAGCTGGGGAAAGAGCTGTGGAGAGAAGAACACCCCAGGGA 1210

QUERY: 1094 TATACACCTCGTTGGTGAACTACAACCTCTGGATCGAGAAAGTGACCCAGCTAGAGGGCA 1153
            |||||||||||||||||||||||||||||||||||||||||| ||||||||||||||||||
SBJCT: 1211 TATACACCTCGTTGGTGAACTACAACCTCTGGATCGAGAAGGTGACCCAGCTAGAGGGCA 1270
QUERY: 1154 GGCCCTTCAATGCAGAGAAAAGGAGGACTTCTGTCAAACAGAAACCTATGGGCTCCCCAG 1213
            ||||||||| ||| ||||||| |||||| |||||||||||||||||||||||||| ||
SBJCT: 1271 GGCCCTTCAGTGCGGAGAAAATGAGGACCTCTGTCAAACAGAAACCTATGGGCTCCCGAG 1330

QUERY: 1214 TCTCGGGAGTCCCAGAGCCAGGCAGCCCCAGATCCTGGCTCCTGCTCTGTCCCCTGTCCC 1273
            ||||||| |||||||||||||||| ||| ||||||||||||||||||||||||||||||
SBJCT: 1331 TCTCGGGGGTCCCAGAGCCAGGCGGCCTCAGATCCTGGCTCCTGCTCTGTCCCCTGTCCC 1390

QUERY: 1274 ATGTGTTGTTCAGAGCTATTTTGTACTGATAATAAAATAGAGGCTATTCTTTCAACC 1330
            |||||||||||||||||||||||||||||||||||||||||||||||||| ||| ||||
SBJCT: 1391 ATGTGTTGTTCAGAGCTATTTTGTACTGATAATAAAATAGAGGCTATTTTTTTAACC 1447

 SCORE =  428 BITS (216), EXPECT = E-117
 IDENTITIES = 346/388 (89%), GAPS = 1/388 (0%)
 STRAND = PLUS / PLUS

QUERY: 1   GATTTTAGAAGGTTAATCAAAAACCCGGGGACAGTTTCTTCATGGCATAACCACAGACCT 60
           |||||||||||||||||||||||||  ||||||||| ||||| |||||||| |||||
SBJCT: 127 GATTTTAGAAGGTTAATCAAAAACCCAAGGACAGTTTCATCATGTCATAACCAAAGACCC 186

QUERY: 61  TTGTGGCACCCGCTGTCGTGGGATATCAAATATCCTCTGGGGTTCGGAATGTGGGCTTAT 120
           |||||||||| |||||| ||||||| |||||||| | |||||||| |||||||| |||||
SBJCT: 187 TTGTGGCACCTGCTGTCATGGGATAACAAATATCTTGTGGGGTTCTGAATGTGGACTTAT 246

QUERY: 121 TACTGAAGATCCTGTCTGCTTGGTCAGTGGCAGGTCTAGACTAACTTCTGGTCCTGAGTT 180
           |||||||| ||||||||||||||||||||  |||||||||||||||||||||||||| |
SBJCT: 247 TACTGAAGCTCCTGTCTGCTTGGTCAGTGG-TGGTCTAGACTAACTTCTGGTCCTGAGAT 305

QUERY: 181 TCTAAAGTGCTGGTAGACCAGTTGATACAAAACAGATATAATAATGAATGCCTTATCTAT 240
           ||||||||| ||||||||| ||||| | |||| | |||||||||||||||||| ||||
SBJCT: 306 TCTAAAGTGTTGGTAGACCGGTTGAGATAAAAGATATATAATAATGAATGCCTTACCTAT 365

QUERY: 241 CTGAAGGTCAGTTTGATCCGTGCCAAGTGGCTTTTTGTGGGCTGTGTAGAGTGCTCTAAA 300
```

```
SBJCT: 366 CTGAAAACC[redacted]TGATCCGTGCCAAGGGGCTTTTTGTGGGCTCTC[redacted]GTGCCCTAAA 425

QUERY: 301 CCCAGCTCGGCCTTTGCTGTATTAGACAGAAGCACCTCATTCATATCCCTGGGGCCCCTG 360
SBJCT: 426 CCCAGCTCTGCCTTTGCTGTGTTAGACAGAAGCACGCCATTCACATCTCTGGGGCCCCCA 485

QUERY: 361 ATGGTGCAGTGGTCTGGCTGTGGTCTGC 388
SBJCT: 486 ATGGTGCCATGGTGTGGTTGTGGTCTGC 513
```

In a search of sequence databases, it was found, for example, that the FCTR6a nucleic acid sequence has 295 of 378 bases (78 %) identical to bases 410-779 of *Mus musculus* adult male testis cDNA, RIKEN full-length enriched (GENBANK-ID:AK09660) (Table 6F).

Table 6F. BLASTN of FCTR6a against *Mus musculus* adult male testis cDNA, RIKEN full-length enriched (SEQ ID NO:83)

```
>GI|12855429|DBJ|AK016601.1|AK016601 MUS MUSCULUS ADULT MALE TESTIS CDNA, RIKEN FULL-
LENGTH ENRICHED
           LIBRARY, CLONE:4933401F05, FULL INSERT SEQUENCE
         LENGTH = 1047

 SCORE = 97.6 BITS (49), EXPECT = 2E-17
 IDENTITIES = 295/378 (78%), GAPS = 8/378 (2%)
 STRAND = PLUS / PLUS

QUERY: 697  AACATGGACAATGACATTGCCTTGCTGCTGCTGGCTTCGCCCATCAAGCTCGATGACCTG 756
SBJCT: 410  AACATGGACAACGACATTGCCTTGTTGCTGCTAGCCAAGCCCTTGACGTTCAATGAGCTG 469

QUERY: 757  AAGGTGCCCATCTGCCTCCCCACGCAGCCCGGCCCTGCCACATGGCGCGAATGCTGGGTG 816
SBJCT: 470  ACGGTGCCCATCTGCCTTCCTCTCTGGCCCGCCCCTCCCAGCTGGCACGAATGCTGGGTG 529

QUERY: 817  GCAGGTTGGGGCCAGACCAATGCTGCTGACAAAAACTCTGTGAAAACGGATCTGATGAAA 876
SBJCT: 530  GCAGGATGGGGCGTAACCAACTCAACTGACAAGGAATCTATGTCAACGGATCTGATGAAG 589

QUERY: 877  GTGCCAATGGTCATCATGGACTGGGAGGAGTGTTCAAAGATGTTTCCAAAACTTACCAAA 936
SBJCT: 590  GTGCCCATGCGTATCATAGAGTGGGAGGAATGCTTACAGATGTTTCCCAGCCTCACCACA 649

QUERY: 937  AATATGCTGTGTGCCGGATACAAGAATGAGAGCTATGATGCCTGCAAGGGTGACAGTGGG 996
SBJCT: 650  AACATGCTGTGTGCCTCATATGGTAATGAGAGCTACGATGCTTGC--------CAGTGGG 701

QUERY: 997  GGGCCTCTGGTCTGCACCCCAGAGCCTGGTGAGAAGTGGTACCAGGTGGGCATCATCAGC 1056
SBJCT: 702  GGACCGCTTGTCTGCACCACAGATCCTGGCAGTAGGTGGTACCAGGTGGGCATCATCAGC 761

QUERY: 1057 TGGGGAAAGAGCTGTGGA 1074
SBJCT: 762  TGGGGCAAGAGCTGTGGA 779
```

The FCTR6a amino acid has 247 of 267 amino acid residues (92%) identical to, and 251 of 307 residues (94%) positive with, the 267 amino acid hypothetical protein [*Macaca fascicularis*] (GenBank: AB046651) (SEQ ID NO:84) (Table 6G).

Table 6G. BLASTP of FCTR6a and b against hypothetical protein [*Macaca fascicularis*] (SEQ ID NO:84)

```
>GI|9651113|DBJ|BAB03569.1| (AB046651) HYPOTHETICAL PROTEIN [MACACA FASCICULARIS]
          LENGTH = 267

 SCORE =  467 BITS (1202), EXPECT = E-131
 IDENTITIES = 247/267 (92%), POSITIVES = 251/267 (94%)

QUERY: 1   MGFRFLGTANSATFETSLPLPLAPLWFSATSPEELSVVLGTNDLTSPSMEIKEVASIILH 60
          | |||| |||| ||| |||| |||||||||||||||+|||||||||| ||||||||||||
SBJCT: 1   MRFRFLSTANSPTFEASLPLSLAPLWFSATSPEELNVVLGTNDLTSSSMEIKEVASIILH 60

QUERY: 61  KDFKRANMDNDIALLLLASPIKLDDLKVPICLPTQPGPATWRECWVAGWGQTNAADKNSV 120
          |||||||||||||||||||| |||||||||||| ||||| ||||||||||||||||||
SBJCT: 61  KDFKRANMDNDIALLLLASPITLDDLKVPICLPTQHGPATWHECWVAGWGQTNAADKNSV 120

QUERY: 121 KTDLMKVPMVIMDWEECSKMFPKLTKNMLCAGYKNESYDACKGDSGGPLVCTPEPGEKWY 180
          |||||| |||||||||||| |||||||||||| |||||||+||||||||||||||||||
SBJCT: 121 KTDLMKAPMVIMDWEECSKAFPKLTKNMLCAGYNNESYDACQGDSGGPLVCTPEPGEKWY 180
                       K                          E
QUERY: 181 QVGIISWGKSCGDKNTPGIYTSLVNYNLWIEKVTQLGGRPFNAEKRRTSVKQKPMGSPVS 240
          ||||||||||||+|||||||||||||||||||||| ||||+||| |||||||||| ||
SBJCT: 181 QVGIISWGKSCGEKNTPGIYTSLVNYNLWIEKVTQLEGRPFSAEKMRTSVKQKPMGSRVS 240

QUERY: 241 GVPEPGSPRSWLLLCPLSHVLFRAILY 267
          ||||||| ||||||||||||||||||||
SBJCT: 241 GVPEPGGLRSWLLLCPLSHVLFRAILY 267

K AND E ARE RESIDUES THAT DIFFER BETWEEN FCTR6A AND B. D193K, AND G217E.
```

The FCTR6a amino acid has 80 of 201 amino acid residues (39%) identical to, and 119 of 201 residues (58%) positive with, the 638 amino acid plasma kallikrein B1 precursor (GENBANK-ID:NP_000883.1) (SEQ ID NO:85) (Table 6H).

Table 6H. BLASTP of FCTR6a and b against plasma kallikrein B1 precursor (SEQ ID NO:85)

```
>GI|4504877|REF|NP_000883.1| PLASMA KALLIKREIN B1 PRECURSOR; KALLIKREIN, PLASMA;
KALLIKREIN B
          PLASMA; KALLIKREIN 3, PLASMA; FLETCHER FACTOR [HOMO
          SAPIENS]
 GI|125184|SP|P03952|KAL_HUMAN PLASMA KALLIKREIN PRECURSOR (PLASMA PREKALLIKREIN)
(KININOGENIN)
          (FLETCHER FACTOR)
 GI|67591|PIR||KQHUP PLASMA KALLIKREIN (EC 3.4.21.34) PRECURSOR - HUMAN
 GI|190263|GB|AAA60153.1| (M13143) PLASMA PREKALLIKREIN [HOMO SAPIENS]
 GI|8809781|GB|AAF79940.1| (AF232742) PLASMA KALLIKREIN PRECURSOR [HOMO SAPIENS]
          LENGTH = 638

 SCORE =  133 BITS (334), EXPECT = 3E-30
 IDENTITIES = 80/201 (39%), POSITIVES = 119/201 (58%), GAPS = 18/201 (8%)

QUERY: 20  LPLAPLWFSATSPEELSVVLGTNDLT--SPSMEIKEVASIILHKDFKRANMDNDIALLLL 77
          |||  +|          | +|  +|+|  +|  +|||   ||+|+++| +  ++||||+ |
SBJCT: 439 LPLQDVW------RIYSGILNLSDITKDTPFSQIKE---IIIHQNYKVSEGNHDIALIKL 489

QUERY: 78  ASPIKLDDLKVPICLPTQPGPAT-WRECWVAGWGQTNAADKNSVKTDLMKVPMVIMDWEE 136
           +|+   + + |||||++   +| +  ||| ||| +   +|  ++  | || + ++  ||
SBJCT: 490 QAPLNYTEFQKPICLPSKGDTSTIYTNCWVTGWGFSK--EKGEIQNILQKVNIPLVTNEE 547
                                                              K
QUERY: 137 CSKMFP--KLTKNMLCAGYKNESYDACKGDSGGPLVCTPEPGEKWYQVGIISWGKSCGDK 194
```

```
SBJCT: 548 CQKRYQDYK[redacted]MVCAGYKEGGKDACKGDSGGPLVC--KHNGMWR[redacted]TSWGEGCARR 605

QUERY: 195 NTPGIYTSLVNYNLWIEKVTQ 215
SBJCT: 606 EQPGVYTKVAEYMDWILEKTQ 626

K IS A RESIDUE THAT DIFFERS BETWEEN FCTR6A AND B. D193K.
```

The FCTR6a amino acid has 73 of 183 amino acid residues (39%) identical to, and 110 of 183 residues (59%) positive with, the 643 amino acid kallikrein [*Sus scrofa*] (GENBANK-ID:BAA37147.1) (SEQ ID NO:86) (Table 6I).

Table 6I. BLASTP of FCTR6a and b against kallikrein [*Sus scrofa*] (SEQ ID NO:86)

```
>GI|4165315|DBJ|BAA37147.1| (AB022425) KALLIKREIN [SUS SCROFA]
          LENGTH = 643

 SCORE =  128 BITS (322), EXPECT = 9E-29
 IDENTITIES = 73/183 (39%), POSITIVES = 110/183 (59%), GAPS = 12/183 (6%)

QUERY: 38  VLGTNDLT--SPSMEIKEVASIILHKDFKRANMDNDIALLLLASPIKLDDLKVPICLPTQ 95
SBJCT: 459 ILNISEITKETPFSQVKE---IIIHQNYKILESGHDIALLKLETPLNYTDFQKPICLPSR 515

QUERY: 96  PGP-ATWRECWVAGWGQTNAADKNSVKTDLMKVPMVIMDWEECSKMFP--KLTKNMLCAG 152
SBJCT: 516 DDTNVVYTNCWVTGWGFTE--EKGEIQNILQKVNIPLVSNEECQKSYRDHKISKQMICAG 573
                                                    K
QUERY: 153 YKNESYDACKGDSGGPLVCTPEPGEKWYQVGIISWGKSCGDKNTPGIYTSLVNYNLWIEK 212
SBJCT: 574 YKEGGKDACKGESGGPLVC--KYNGIWHLVGTTSWGEGCARREQPGVYTKVIEYMDWILE 631

QUERY: 213 VTQ 215
SBJCT: 632 KTQ 634

K IS A RESIDUE THAT DIFFERS BETWEEN FCTR6A AND B. D193K.
```

The FCTR6a amino acid has 81 of 205 amino acid residues (39%) identical to, and 112 of 205 residues (54%) positive with, the 625 amino acid Coagulation factor XI [*Homo sapiens*] (embCAA64368.1) (SEQ ID NO:87) (Table 6J).

Table 6J. BLASTP of FCTR6a and b against Coagulation factor XI [*Homo sapiens*] (SEQ ID NO:87)

```
>GI|180352|GB|AAA51985.1| (M20218) COAGULATION FACTOR XI [HOMO SAPIENS]
          LENGTH = 625

 SCORE =  127 BITS (320), EXPECT = 1E-28
 IDENTITIES = 81/205 (39%), POSITIVES = 112/205 (54%), GAPS = 17/205 (8%)

QUERY: 20  LPLAPLWFSATSPEELSVVLGTNDLTSPSMEIKE------VASIILHKDFKRANMDNDIA 73
SBJCT: 427 LTAAHCFYGVESPKILRVYSGILNQS----EIKEDTSFFGVQEIIIHDQYKMAESGYDIA 482

QUERY: 74  LLLLASPIKLDDLKVPICLPTQPG-PATWRECWVAGWGQTNAADKNSVKTDLMKVPMVIM 132
SBJCT: 483 LLKLETTVNYTDSQRPICLPSKGDRNVIYTDCWVTGWGYRKLRDK--IQNTLQKAKIPLV 540

QUERY: 133 DWEECSKMFP--KLTKNMLCAGYKNESYDACKGDSGGPLVCTPEPGEKWYQVGIISWGKS 190
```

```
                |||  | +   |+|  |+||||+    |||||||||||  |  +  |||+ |||  |||+
SBJCT: 541 TNEECQKRYF    ITHKMICAGYREGGKDACKGDSGGPLSC--KHN    LVGITSWGEG 598
                 K
QUERY: 191 CGDKNTPGIYTSLVNYNLWIEKVTQ 215
           |  +  ||+||++|  |   || + ||
SBJCT: 599 CAQRERPGVYTNVVEYVDWILEKTQ 623

K IS A RESIDUE THAT DIFFERS BETWEEN FCTR6A AND B. D193K.
```

The number of new cases of renal cell carcinoma in the United States in 1996 was projected to be 30,600 with an estimated 12,000 deaths. Tumors with a proposed histogenesis from the proximal tubule (clear-cell and chromophilic tumors) amount to 85% of renal cancers, whereas tumors with a proposed histogenesis from the connecting tubule/collecting duct (chromophobic-, oncocytic-, and duct Bellini-type tumors) amount to only 11%.

Adenocarcinomas may be separated into clear cell and granular cell carcinomas, although the 2 cell types may occur together in some tumors. The distinction between well-differentiated renal carcinomas and renal adenomas can be difficult. The diagnosis is usually made arbitrarily on the basis of size of the mass, but size alone should not influence the treatment approach, since metastases can occur with lesions as small as 0.5 centimeters.

While radical nephrectomy with regional lymphadenectomy, is the accepted, often curative therapy for stage I (localized disease) renal cell cancer, very little therapy is available for advance disease that represent about 70% of the patients. Radiotherapy as a postoperative adjuvant has not been effective, and when used preoperatively, may decrease local recurrence but does not appear to improve 5-yr survival. A chemotherapeutic agent capable of significantly altering the course of metastastic renal cell carcinoma has not been identified. (Renal Cell Cancer (PDQ®) Treatment - Health Professionals, Cancernet, NCI)

There is therefore a need to identify genes that are differentially modulated in renal-cell carcinomas. In addition there is a need for methods to assay candidate therapeutic substances for modulating expression of these genes. These substances might be recombinant protein expressed by the identified genes or antibodies that bind to the identified proteins. There is yet additionally a need for an effective method of identifying target molecules or related components. These and related needs and defects are addressed in the present invention.

Novel kallikrein-like/coagulation factor XI-like Proteins and Nucleic Acids Encoding Same

FCTR6 is surprisingly found to be differentially expressed in clear cell Renal cell carcinoma tissues vs the normal adjacent kidney tissues. The present invention discloses a novel protein encoded by a cDNA and/or by genomic DNA and proteins similar to it, namely, new proteins bearing sequence similarity to kallikrein-like, nucleic acids that encode these proteins or

fragments thereof, and antibodies that bind immunospecifically to protein of the invention. It may have use as a therapeutic agent in the treatmentof renal cancer and liver cirrhosis.

The utility of kallikrein family members in protein therapy of Renal cancer

The treatment of renal cell carcinoma with recombinant kallikrein could improve disease outcome through several potential mechanisms. The literature suggests that members of this protein family are inhibitory to the process of angiogenesis, a process of vital importance to tumor progression. Renal cell carcinoma is known to be a highly angiogenic cancer. Thus, treatment of renal cell carcinoma with kallikrein may effectively shutdown the active recruitment of a blood supply to a tumor. Members of this protein family are known to play a role in vascular coagulation. Similar to anti-angiogenic therapy, a factor produced by cancer cells that is pro-coagulatory may also act to inhibit cancer growth by effectively "clogging" the tumor vascular supply. In addition, through its proteolytic activity, kallikrein may degrade ECM proteins or growth factors necessary for the progressive growth of cancer cells. Following is a relevant reference underlining the importance of Kallikrein in cancer therapy.

The New Human Kallikrein Gene Family: Implications in Carcinogenesis.

Diamandis EP; Yousef GM; Luo I; Magklara I; Obiezu CV

Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Ontario, Canada.

Trends Endocrinol Metab 2000 Mar;11(2):54-60.

ABSTRACT: The traditional human kallikrein gene family consists of three genes, namely KLK1 [encoding human kallikrein 1 (hK1) or pancreatic/renal kallikrein], KLK2 (encoding hK2, previously known as human glandular kallikrein 1) and KLK3 [encoding hK3 or prostate-specific antigen (PSA)]. KLK2 and KLK3 have important applications in prostate cancer diagnostics and, more recently, in breast cancer diagnostics. During

the past two to three years, new putative members of the human kallikrein gene family have been identified, including the PRSSL1 gene [encoding normal epithelial cell-specific 1 gene (NES1)], the gene encoding zyme/protease M/neurosin, the gene encoding prostase/KLK-L1, and the genes encoding neuropsin, stratum corneum chymotryptic enzyme and trypsin-like serine protease. Another five putative kallikrein genes, provisionally named KLK-L2, KLK-L3, KLK-L4, KLK-L5 and KLK-L6, have also been identified. Many of the newly identified kallikrein-like genes are regulated by steroid hormones, and a few kallikreins (NES1, protease M, PSA) are known to be downregulated in breast and possibly other cancers. NES1 appears to

be a novel breast cancer tumor suppressor protein and PSA a potent inhibitor of angiogenesis. This brief review summarizes recent developments and possible applications of the newly defined and expanded human kallikrein gene locus.

The utility of kallikrein-like/coagulation factor XI-like family members in protein therapy of liver cirrosis

Results related to inflammation shown below in Example A, Table CC3, panel 4, indicate over-expression of 27455183.0.19 in the liver cirrhosis sample, as compared to panel 1 data (Table CC1), where there is little or no expression in normal adult liver. Panel 4 was generated from various human cell lines that were untreated or resting as well as the same cells that were treated with a wide variety of immune modulatory molecules. There are several disease tissues represented as well as organ controls.

Potential Role(s) of FCTR6 in Inflammation:

Liver cirrhosis occurs in patients with hepatitis C and also in alcoholics. This protein is 41% related to coagulation factor XI and its potential role in liver cirrhosis may be related to cleavage of kininogen. A reference for this follows:

Thromb Haemost 2000 May;83(5):709-14 High molecular weight kininogen is cleaved by FXIa at three sites: Arg409-Arg410, Lys502-Thr503 and Lys325-Lys326. Mauron T, Lammle B, Wuillemin WA Central Hematology Laboratory, University of Bern, Inselspital, Switzerland. Abstract:

We investigated the cleavage of high molecular weight kininogen (HK) by activated coagulation factor XI (FXIa) in vitro. Incubation of HK with FXIa resulted in the generation of cleavage products which were subjected to SDS-Page and analyzed by silverstaining, ligand-blotting and immunoblotting, respectively. Upon incubation with FXIa, bands were generated at 111, 100, 88 kDa on nonreduced and at 76, 62 and 51 kDa on reduced gels. Amino acid sequence analysis of the reaction mixtures revealed three cleavage sites at Arg409-Arg410, at Lys502-Thr503 and at Lys325-Lys326. Analysis of HK-samples incubated with FXIa for 3 min, 10 min and 120 min indicated HK to be cleaved first at Arg409-Arg410, followed by cleavage at Lys502-Thr503 and then at Lys325-Lys326. In conclusion, HK is cleaved by FXIa at three sites. Cleavage of HK by FXIa results in the loss of the surface binding site of HK, which may constitute a mechanism of inactivation of HK and of control of contact system activation.

Impact of Therapeutic Targeting of FCTR6 in Inflammation:

Therapeutic targeting of FCTR6 with a monoclonal antibody is anticipated to limit or block the extent of breakdown of kininogen and thereby reduce the degradation of liver that occurs in liver cirrhosis. A pertinent reference is:

Thromb Haemost 1999 Nov;82(5):1428-32 Parallel reduction of plasma levels of high and low molecular weight kininogen in patients with cirrhosis.

Cugno M, Scott CF, Salerno F, Lorenzano E, Muller-Esterl W, Agostoni A, Colman RW

Department of Internal Medicine, IRCCS Maggiore Hospital, University of Milan, Italy. massimo.cugno@unimi.it

Abstract:

Little is known about the regulation of high-molecular-weight-kininogen (HK) and low-molecular-weight-kininogen (LK) or the relationship of each to the degree of liver function impairment in patients with cirrhosis. In this study, we evaluated HK and LK quantitatively by a recently described particle concentration fluorescence immunoassay (PCFIA) and qualitatively by SDS PAGE and immunoblotting analyses in plasma from 33 patients with cirrhosis presenting various degrees of impairment of liver function. Thirty-three healthy subjects served as normal controls. Patients with cirrhosis had significantly lower plasma levels of HK (median 49 microg/ml [range 22-99 microg/ml]) and LK (58 microg/ml [15-100 microg/ml]) than normal subjects (HK 83 microg/ml [65-115 microg/ml]; LK 80 microg/ml [45-120 microg/ml]) ($p<0.0001$). The plasma concentrations of HK and LK were directly related to plasma levels of cholinesterase ($P<0.0001$) and albumin ($P<0.0001$ and $P<0.001$) and inversely to the Child-Pugh score ($P<0.0001$) and to prothrombin time ratio ($P<0.0001$) (reflecting the clinical and laboratory abnormalities in liver disease). Similar to normal individuals, in patients with cirrhosis, plasma HK and LK levels paralleled one another, suggesting that a coordinate regulation of those proteins persists in liver disease. SDS PAGE and immunoblotting analyses of kininogens in cirrhotic plasma showed a pattern similar to that observed in normal controls for LK (a single band at 66 kDa) with some lower molecular weight forms noted in cirrhotic plasma. A slight increase of cleavage of HK (a major band at 130 kDa and a faint but increased band at 107 kDa) was evident. The increased cleavage of HK was confirmed by the lower cleaved kininogen index (CKI), as compared to normal controls. These data suggest a defect in hepatic synthesis as well as increased destructive cleavage of both kininogens in plasma from patients with cirrhosis. The decrease of important regulatory proteins like kininogens may contribute to the imbalance in coagulation and fibrinolytic systems, which frequently occurs in cirrhotic patients.

In summary, the differential expression of FCTR6 (Kallikrein family) in renal cell carcinoma is an important finding that could have immense potential in renal carcinogenesis. In

additon, overexpression of the above gene in liver cirrhosis demonstrates its anticipated use as an immunotherapeutic target.

FCTR7

The novel nucleic acid of 1498 nucleotides FCTR7 (also designated. 32592466.0.64) encoding a novel trypsin inhibitor-like protein is shown in Table 7A. An ORF begins with an ATG initiation codon at nucleotides 470-472 and ends with a TAA codon at nucleotides 1369-1371. Putative untranslated regions, if any, are found upstream from the initiation codon and downstream from the termination codon.

Table 7A. FCTR7 Nucleotide Sequence (SEQ ID NO:24)

AGGCGCCTGGTTCTGCGCGTACTGGCTGTACGGAGCAGGAGCAAGAGGTCGCCGCCAGCCTCCGCCGCCGAGCCTCGTTCGTGTCC
CCGCCCCTCGCTCCTGCAGCTACTGCTCAGAAACGCTGGGGCGCCCACCCTGGCAGACTAACGAAGCAGCTCCCTTCCCACCCCAA
CTGCAGGTCTAATTTTGGACGCTTTGCCTGCCATTTCTTCCAGGTTGAGGGAGCCGCAGAGGCGGAGGCTCGCGTATTCCTGCAGT
CAGCACCCACGTCGCCCCCGGACGCTCGGTGCTCAGGCCCTTCGCGAGCGGGGCTCTCCGTCTGCGGTCCCTTGTGAAGGCTCTGG
GCGGCTGCAGAGGCCGGCCGTCCGGTTTGGCTCACCTCTCCCAGGAAACTTCACACTGGAGAGCCAAAAGGAGTGGAAGAGCCTGT
CTTGGAGATTTTCCTGGGGAAATCCTGAGGTCATTCATT**ATG**AAGTGTACCGCGCGGGAGTGGCTCAGAGTAACCACAGTGCTGTT
CATGGCTAGAGCAATTCCAGCCATGGTGGTTCCCAATGCCACTTTATTGGAGAAACTTTTGGAAAAATACATGGATGAGGATGGTG
AGTGGTGGATAGCCAAACAACGAGGGAAAAGGGCCATCACAGACAATGACATGCAGAGTATTTTGGACCTTCATAATAAATTACGA
AGTCAGGTGTATCCAACAGCCTCTAATATGGAGTATATGACATGGGATGTAGAGCTGGAAAGATCTGCAGAATCCAGGGCTGAAAT
TGCTTGTGGGAACATGGACCTGCAAGCTTGCTTCCATCAATTGGACAGAATTTGGGAGCACACTGGGGAAGATATAGGCCCCCGAC
GTTTCATGTACAATCGTGGTATGATGAAGTGAAAGACTTTAGCTACCCATATGAACATGAATGCAACCCATATTGTCCATTCAGGT
GTTCTGGCCCTGTATGTACACATTATACACAGGTCGTGTGGGCAACTAGTAACAGAATCGGTTGTGCCATTAATTTGTGTCATAAC
ATGAACATCTGGGGGCAGATATGGCCCAAAGCTGTCTACCTGGTGTGCAATTACTCCCCAAAGGGAAACTGGTGGGGCCATGCCCC
TTACAAACATGGGCGGCCCTGTTCTGCTTGCCCACCTAGTTTTGGAGGGGGCTGTAGAGAAAATCTGTGCTACAAAGAAGGGTCAG
ACAGGTATTATCCCCCTCGAGAAGAGGAAACAAATGAAATAGAACGGCAGCAGTCACAAGTCCATGACACCCATGTCCGGACAAGA
TCAGATGATAGTAGCAGAAATGAAGTCATTAGCTTTGGGAAAAGTAATGAAAATATAATGGTTTTAGAAATCCTGTGT**TAA**ATATT
GCTATATTTTCTTAGCAGTTATTTCTACAGTTAATTACATAGTCATGATTGTTCTACGTTTCATATATTATATGGTGCTTTGTATA
TGCCCCTAATAAAATGAATCTAAACATTGAAAAAAA

The FCTR7 protein encoded by SEQ ID NO:24 has 300 amino acid residues and is presented using the one-letter code in Table 7B. The FCTR7 gene was found to be expressed in: brain; germ cell tumors. FCTR7 gene maps to Unigene cluster Hs.182364 which is expressed in the following tissues: brain, breast, ear, germ cell, heart, liver, lung, whole embryo, ovary, pancreas, pooled, prostate, stomach, testis, uterus, vascular. Therefore the FCTR7 protein described in this invention is also expressed in the above tissues.

The SignalP, Psort and/or Hydropathy profile for FCTR7 predict that this sequence has a signal peptide and is likely to be localized outside of the cell with a certainty of 0.4228. The SignalP shows a cleavage site between amino acids 20 and 21, *i.e.*, at the dash in the sequence amino acid ARA-IP. The predicted molecular weight of FCTR7 is 34739.9 Daltons. Hydropathy profile shows an amino terminal hydrophobic region. This region could function as a signal peptide and target the invention to be secreted or plasma membrane localized.

Table 7B. Encoded FCTR7 protein sequence (SEQ ID NO:25).

MKCTAREWLRVTTVLFMARA[redacted]VVPNATLLEKLLEKYMDEDGEWWIAKQRGKRAI[redacted]DMQSILDLHNKLRSQVYPTASNMEYM
TWDVELERSAESRAESCLWEHGPASLLPSIGQNLGAHWGRYRPPTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVV
WATSNRIGCAINLCHNMNIWGQIWPKAVYLVCNYSPKGNWWGHAPYKHGRPCSACPPSFGGGCRENLCYKEGSDRYYPPREEETNE
IERQQSQVHDTHVRTRSDDSSRNEVISFGKSNENIMVLEILC

This gene maps to Unigene cluster Hs.182364 which has been assigned the following mapping information shown in table 7C. Therefore the chromosomal assignment for this gene is the same as that for Unigene cluster 182364.

Table 7C. Mapping Information.

Chromosome:	8
Gene Map 98:	Marker SHGC-32056 , Interval D8S279-D8S526
Gene Map 98:	Marker SGC32056 , Interval D8S526-D8S275
Gene Map 98:	Marker sts-G20223 , Interval D8S526-D8S275
Gene Map 98:	Marker stSG30385 , Interval D8S526-D8S275
Whitehead map:	EST67946, Chr.8
dbSTS entries:	G25853, G29349, G20223

The predicted amino acid sequence was searched in the publicly available GenBank database

FCTR7 protein showed Score = 743 (261.5 bits), Expect = 1.4e-73, P = 1.4e-73, 54 % identities (129 over 237 amino acids) and 43% homologies (167 over 237 amino acids) with human 25 kD trypsin inhibitor protein (258 aa; ACC:O43692) (Table 7D).

Table 7D. BLAST X search results are shown below:

ptnr:SPTREMBL-ACC:O43692 25 KDA TRYPSIN INHIBITOR - HO... +2 743 8.4e-73 1 (SEQ ID NO:88)

ptnr:SPTREMBL-ACC:O44228 HRTT-1 - HALOCYNTHIA RORETZI ... +2 325 2.9e-28 1 (SEQ ID NO:89)

ptnr:SWISSPROT-ACC:P48060 GLIOMA PATHOGENESIS-RELATED ... +2 314 5.3e-27 1 (SEQ ID NO:90)

ptnr:PIR-ID:JC4131 glioma pathogenesis-related protein... +2 309 2.0e-26 1 (SEQ ID NO:91)

ptnr:SWISSNEW-ACC:O19010 CYSTEINE-RICH SECRETORY PROTE... +2 258 9.4e-21 1 (SEQ ID NO:92)

The nucleotide sequence of FCTR7 has 954 of 957 residues (99 %) identical to the 1-957 base segment, and 174 of 175 residues (99%) identical to bases 1317-1953 of the 2664

nucleotide *Homo sapiens* putative secretory protein precursor, mRNA (GenBank-ACC: AF142573) (SEQ ID NO:93) (Table 7E).

Table 7E. BLASTN of FCTR7 against Putative secretory protein precursor (SEQ ID NO:93)

```
>gi|12002310|gb|AF142573.1|AF142573 Homo sapiens putative secretory protein
precursor, mRNA, complete cds
          Length = 2664

 Score = 1865 bits (941), Expect = 0.0
 Identities = 954/957 (99%), Gaps = 1/957 (0%)
 Strand = Plus / Plus

Query: 364  gtccggtttggctcacctctcccaggaaacttcacactggagagccaaaaggagtggaag 423
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 1    gtccggtttggctcacctctcccaggaaacttcacactggagagccaaaaggagtggaag 60

Query: 424  agcctgtcttggagattttcctggggaaatcctgaggtcattcattatgaagtgtaccgc 483
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 61   agcctgtcttggagattttcctggggaaatcctgaggtcattcattatgaagtgtaccgc 120

Query: 484  gcgggagtggctcagagtaaccacagtgctgttcatggctagagcaattccagccatggt 543
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 121  gcgggagtggctcagagtaaccacagtgctgttcatggctagagcaattccagccatggt 180

Query: 544  ggttcccaatgccactttattggagaaacttttggaaaaatacatggatgaggatggtga 603
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 181  ggttcccaatgccactttattggagaaacttttggaaaaatacatggatgaggatggtga 240

Query: 604  gtggtggatagccaaacaacgagggaaaagggccatcacagacaatgacatgcagagtat 663
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 241  gtggtggatagccaaacaacgagggaaaagggccatcacagacaatgacatgcagagtat 300

Query: 664  tttggaccttcataataaattacgaagtcaggtgtatccaacagcctctaatatggagta 723
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 301  tttggaccttcataataaattacgaagtcaggtgtatccaacagcctctaatatggagta 360

Query: 724  tatgacatgggatgtagagctggaaagatctgcagaatccagggctgaaa-ttgcttgtg 782
             |||||||||||||||||||||||||||||||||| ||||||||| |||||||||
Sbjct: 361  tatgacatgggatgtagagctggaaagatctgcagaatcctgggctgaaagttgcttgtg 420

Query: 783  ggaacatggacctgcaagcttgcttccatcaattggacagaatttgggagcacactgggg 842
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 421  ggaacatggacctgcaagcttgcttccatcaattggacagaatttgggagcacactgggg 480

Query: 843  aagatataggcccccgacgtttcatgtacaatcgtggtatgatgaagtgaaagactttag 902
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 481  aagatataggcccccgacgtttcatgtacaatcgtggtatgatgaagtgaaagactttag 540

Query: 903  ctacccatatgaacatgaatgcaacccatattgtccattcaggtgttctggccctgtatg 962
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 541  ctacccatatgaacatgaatgcaacccatattgtccattcaggtgttctggccctgtatg 600

Query: 963  tacacattatacacaggtcgtgtgggcaactagtaacagaatcggttgtgccattaattt 1022
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 601  tacacattatacacaggtcgtgtgggcaactagtaacagaatcggttgtgccattaattt 660

Query: 1023 gtgtcataacatgaacatctgggggcagatatggcccaaagctgtctacctggtgtgcaa 1082
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 661  gtgtcataacatgaacatctgggggcagatatggcccaaagctgtctacctggtgtgcaa 720
```

```
Query: 1083 ttactc[redacted]aagggaaactggtggggccatgcccctta[redacted]catgggcggccctgttc 1142
           ||||||[redacted]||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 721  ttactccccaaagggaaactggtggggccatgcccctta[redacted]caaacatgggcggccctgttc 780

Query: 1143 tgcttgcccacctagttttggaggggctgtagagaaaatctgtgctacaaagaagggtc 1202
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 781  tgcttgcccacctagttttggaggggctgtagagaaaatctgtgctacaaagaagggtc 840

Query: 1203 agacaggtattatccccctcgagaagaggaaacaaatgaaatagaacggcagcagtcaca 1262
           |||||||||||||||||||||||||||||||||||||||||||||||||||| ||||||||||
Sbjct: 841  agacaggtattatccccctcgagaagaggaaacaaatgaaatagaacgacagcagtcaca 900

Query: 1263 agtccatgacacccatgtccggacaagatcagatgatagtagcagaaatgaagtcat 1319
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 901  agtccatgacacccatgtccggacaagatcagatgatagtagcagaaatgaagtcat 957

Score =  339 bits (171), Expect = 3e-90
 Identities = 174/175 (99%)
 Strand = Plus / Plus

Query: 1317 cattagctttgggaaaagtaatgaaaatataatggttttagaaatcctgtgttaaatatt 1376
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 1779 cattagctttgggaaaagtaatgaaaatataatggttttagaaatcctgtgttaaatatt 1838

Query: 1377 gctatattttcttagcagttatttctacagttaattacatagtcatgattgttctacgtt 1436
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 1839 gctatattttcttagcagttatttctacagttaattacatagtcatgattgttctacgtt 1898

Query: 1437 tcatatattatatggtgctttgtatatgcccctaataaaatgaatctaaacattg 1491
           |||||||||||||||||||||||||||||| ||||||||||||||||||||||
Sbjct: 1899 tcatatattatatggtgctttgtatatgccactaataaaatgaatctaaacattg 1953
```

The FCTR7 amino acid has 284 of 285 amino acid residues (99%) identical to, and 284 of 285 amino acid residues (99%) similar to, the 500 amino acid Putative secretory protein precursor [*Homo sapiens*] (GenBank-Acc No.: AF142573) (SEQ ID NO:94) (Table 7F).

Table 7F. BLASTP alignments of FCTR7 against Putative secretory protein precursor, (SEQ ID NO:94)

```
>gi|12002311|gb|AAG43287.1|AF142573_1 (AF142573) putative secretory protein
precursor [Homo sapiens]
          Length = 500

 Score =  581 bits (1499), Expect = e-165
 Identities = 284/285 (99%), Positives = 284/285 (99%)

Query: 1   MKCTAREWLRVTTVLFMARAIPAMVVPNATLLEKLLEKYMDEDGEWWIAKQRGKRAITDN 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 1   MKCTAREWLRVTTVLFMARAIPAMVVPNATLLEKLLEKYMDEDGEWWIAKQRGKRAITDN 60

Query: 61  DMQSILDLHNKLRSQVYPTASNMEYMTWDVELERSAESRAESCLWEHGPASLLPSIGQNL 120
           |||||||||||||||||||||||||||||||||| ||||||||||||||||||||||||||
Sbjct: 61  DMQSILDLHNKLRSQVYPTASNMEYMTWDVELERSAESWAESCLWEHGPASLLPSIGQNL 120

Query: 121 GAHWGRYRPPTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVVWATSNRIG 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 121 GAHWGRYRPPTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVVWATSNRIG 180

Query: 181 CAINLCHNMNIWGQIWPKAVYLVCNYSPKGNWWGHAPYKHGRPCSACPPSFGGGCRENLC 240
```

```
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 181 CAINLCH[redacted]WGQIWPKAVYLVCNYSPKGNWWGHAPYKH[redacted]SACPPSFGGGCRENLC 240

Query: 241 YKEGSDRYYPPREEETNEIERQQSQVHDTHVRTRSDDSSRNEVIS 285
           |||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 241 YKEGSDRYYPPREEETNEIERQQSQVHDTHVRTRSDDSSRNEVIS 285
```

The FCTR7 amino acid has 137 of 176 amino acid residues (78%) identical to, and 151 of 176 amino acid residues (86%) similar to, the 188 amino acid Late gestation lung protein 1 [*Rattus norvegicus*] (GenBank-Acc No.: AF109674) (SEQ ID NO:95) (Table 7G).

Table 7G. BLASTP alignments of FCTR7 against Late gestation lung protein 1, (SEQ ID NO:95)

```
>gi|4324682|gb|AAD16986.1| (AF109674) late gestation lung protein 1 [Rattus
norvegicus]
          Length = 188

 Score =  277 bits (709), Expect = 1e-73
 Identities = 137/176 (78%), Positives = 151/176 (86%)

Query: 68  LHNKLRSQVYPTASNMEYMTWDVELERSAESRAESCLWEHGPASLLPSIGQNLGAHWGRY 127
           ||||||  ||||  ||||||||||  ||||||    |  ||||||||||  ||||||  |||||
Sbjct: 2   LHNKLRGQVYPPASNMEYMTWDEELERSAAAWAQRCLWEHGPASLLVSIGQNLAVHWGRY 61

Query: 128 RPPTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVVWATSNRIGCAINLCH 187
           | | ||||||||||||++|||  |||||+||  ||||  +||||||+||||+|+||||++ |
Sbjct: 62  RSPGFHVQSWYDEVKDYTYPYPHECNPWCPERCSGAMCTHYTQMVWATTNKIGCAVHTCR 121

Query: 188 NMNIWGQIWPKAVYLVCNYSPKGNWWGHAPYKHGRPCSACPPSFGGGCRENLCYKE 243
           +|++||  ||   |||||||||||||| | ||||||||| || |+|||||  ||||+|
Sbjct: 122 SMSVWGDIWENAVYLVCNYSPKGNWIGEAPYKHGRPCSECPSSYGGGCRNNLCYRE 177
```

The FCTR7 amino acid has 130 of 237 amino acid residues (55%) identical to, and 165 of 237 amino acid residues (70%) similar to, the 258 amino acid R3H domain-containing preproprotein; 25 kDa trypsin inhibitor [*Homo sapiens*] (GenBank-Acc No.: D45027) (SEQ ID NO:96) (Table 7H).

Table 7H. BLASTP alignments of FCTR7 against R3H domain-containing preproprotein, 25 kDa trypsin inhibitor (SEQ ID NO:96)

```
>gi|7705676|ref|NP_056970.1| R3H domain-containing preproprotein; 25 kDa
trypsin inhibitor; R3H
          domain (binds single-stranded nucleic acids) containing
          [Homo sapiens]
 gi|2943716|dbj|BAA25066.1| (D45027) 25 kDa trypsin inhibitor [Homo sapiens]
          Length = 258

 Score =  265 bits (678), Expect = 4e-70
 Identities = 130/237 (55%), Positives = 165/237 (70%), Gaps = 3/237 (1%)

Query: 12  TTVLFMARAIPAMVVPNATLLEKLLEKYMDEDGEWWIAKQRGKRAITDNDMQSILDLHNK 71
           +||+ +     +    | | +|  |+  +|      | | | || |+ ||| +||| ||+
Sbjct: 20  STVVLLNSTDSSPPTNNFTDIEAALKAQLDSAD---IPKARRKRYISQNDMIAILDYHNQ 76
```

```
Query: 72  LRSQVYPTASNMEYMTWDVELERSAESRAESCLWEHGPASLLPSIGQNLGAHWGRYRPPT 131
           +| +|+|[redacted]|||| ||  |  |||  |  |+|+|||+ [redacted]+|||    ||||
Sbjct: 77  VRGKVFPP[redacted]NMEYMVWDENLAKSAEAWAATCIWDHGPSYLLRFLGQNLSVRTGRYRSIL 136

Query: 132 FHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVVWATSNRIGCAINLCHNMNI 191
             |+ |||||||+++||  +||| || || ||+||||||+|||||||||||||+ | |||+
Sbjct: 137 QLVKPWYDEVKDYAFPYPQDCNPRCPMRCFGPMCTHYTQMVWATSNRIGCAIHTCQNMNV 196

Query: 192 WGQIWPKAVYLVCNYSPKGNWWGHAPYKHGRPCSACPPSFGGGCRENLCYKEGSDRY 248
           || +| +|||||||+|||||  | |||| | |||+||||+||  | +|||+   +  |
Sbjct: 197 WGSVWRRAVYLVCNYAPKGNWIGEAPYKVGVPCSSCPPSYGGGSCTDNLCFPGVTSNY 253
```

The FCTR7 amino acid has 109 of 233 amino acid residues (47%) identical to, and 146 of 233 amino acid residues (63%) similar to, the 253 amino acid Novel protein similar to a trypsin inhibitor [*Homo sapiens*] 25 kDa trypsin inhibitor (EMBLAcc No.: AL117382) (SEQ ID NO:97) (Table 7I).

Table 7I. BLASTP alignments of FCTR7 against Novel protein similar to a trypsin inhibitor, (SEQ ID NO:97)

```
>gi|9885193|emb|CAC04190.1| (AL117382) dJ881L22.3 (novel protein similar to a
trypsin
           inhibitor) [Homo sapiens]
          Length = 253

 Score =  225 bits (575), Expect = 4e-58
 Identities = 109/233 (47%), Positives = 146/233 (63%), Gaps = 8/233 (3%)

Query: 10  RVTTVLFMARAIPAMVVPNATLLEKLLEKYMDEDGEWWIAKQRGKRAITDNDMQSILDLH 69
           +    | |  | ||   | +| +  |            + + | || |+  || ++|| |
Sbjct: 19  QAVNALIMPNATPAPAQPESTAMRLL--------SGLEVPRYRRKRHISVRDMNALLDYH 70

Query: 70  NKLRSQVYPTASNMEYMTWDVELERSAESRAESCLWEHGPASLLPSIGQNLGAHWGRYRP 129
           | +|+ ||| |+|||||  ||  | | ||  |  |+| |||+ |+  +||||  | |+||
Sbjct: 71  NHIRASVYPPAANMEYMVWDKRLARAAEAWATQCIWAHGPSQLMRYVGQNLSIHSGQYRS 130

Query: 130 PTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVVWATSNRIGCAINLCHNM 189
               ++|| +|   + +|   +|||+||+|| || |+||||+|||+|||+||||+ | ++
Sbjct: 131 VVDLMKSWSEEKWHYLFPAPRDCNPHCPWRCDGPTCSHYTQMVWASSNRLGCAIHTCSSI 190

Query: 190 NIWGQIWPKAVYLVCNYSPKGNWWGHAPYKHGRPCSACPPSFGGGCRENLCYK 242
           ++||  | +| ||||||+ |||| | +||| |+|||+||||+ | |  |+|+|
Sbjct: 191 SVWGNTWHRAAYLVCNYAIKGNWIGESPYKMGKPCSSCPPSYQGSCNSNMCFK 243
```

The FCTR7 amino acid has 129 of 237 amino acid residues (54%) identical to, and 167 of 237 amino acid residues (70%) similar to, the 258 amino acid 25 kDa Trypsin Inhibitor from *Homo sapiens* (EMBLAcc No.: O43692) (SEQ ID NO:88) (Table 7J).

Table 7J. BLASTP alignments of FCTR7 against 25 kDa Trypsin Inhibitor, (SEQ ID NO:88)

```
ptnr:SPTREMBL-ACC:O43692 25 KDA TRYPSIN INHIBITOR - Homo sapiens (Human), 258
aa.
Score = 743 (261.5 bits), Expect = 1.6e-73, P = 1.6e-73
 Identities = 129/237 (54%), Positives = 167/237 (70%)
```

The FCTR7 amino acid has 79 of 193 amino acid residues (40%) identical to, and 110 of 193 amino acid residues (56%) similar to, the 266 amino acid Glioma Pathogenesis-Related Protein (RTVP-1 Protein) - *Homo sapiens* (SWISSPROT Acc No.: P48060) (SEQ ID NO:90) (Table 7K).

Table 7K. BLASTP alignments of FCTR7 against Glioma Pathogenesis-Related Protein, (SEQ ID NO:90)

```
ptnr:SWISSPROT-ACC:P48060 GLIOMA PATHOGENESIS-RELATED PROTEIN (RTVP-1 PROTEIN)
- Homo sapiens (Human), 266 aa
Score = 314 (110.5 bits), Expect = 4.7e-28, P = 4.7e-28
 Identities = 79/193 (40%), Positives = 110/193 (56%)
```

The FCTR7 amino acid has 66 of 186 amino acid residues (35%) identical to, and 91 of 186 amino acid residues (48%) similar to, the 186 amino acid Neutrophil granules matrix glycoprotein SGP28 precursor from *Homo sapiens* (SWISSPROT Acc No.: S68691) (SEQ ID NO:98) (Table 7L).

Table 7L. BLASTP alignments of FCTR7 against Neutrophil granules matrix glycoprotein, (SEQ ID NO:98)

```
ptnr:PIR-ID:S68691 neutrophil granules matrix glycoprotein SGP28 precursor -
human
Score = 254 (89.4 bits), Expect = 1.1e-21, P = 1.1e-21
 Identities = 66/186 (35%), Positives = 91/186 (48%)
```

A novel developmentally regulated gene with homology to a tumor derived trypsin inhibitor is expressed in lung mesenchyme, as described in Am. J. Physiol. 0:0-0(1999). cDNA cloning of a novel trypsin inhibitor with similarity to pathogenesis-related proteins, and its frequent expression in human brain cancer cells is disclosed in Biochim. Biophys. Acta 1395:202-208(1998). RTVP-1, a novel human gene with sequence similarity to genes of diverse species, is expressed in tumor cell lines of glial but not neuronal origin, as published in Gene 180:125-130(1996). The human glioma pathogenesis-related protein is structurally related to plan pathogenesis-related proteins and its gene is expressed specifically in brain tumors (Gene 159:131-135(1995)). Structure comparison of human glioma pathogenesis-related protein GliPR and the plant pathogenesis-related protein P14a indicates a functional link between the human

immune system and a plant defense system (Proc. Natl. Acad. Sci. U.S.A. 95:2262-2266(1998)). GliPR is highly expressed in the human brain tumor, glioblastoma multiform/astrocytome, but neither in normal fetal or adult brain tissue, nor in other nervous system tumors. GliPR belongs to a family that groups mammalian SCP/TPX1; insects AG3/AG5; FUNGI SC7/SC14 and plants PR-1. SGP28, a novel matrix glycoprotein in specific granules of human neutrophils with similarity to a human testis-specific gene product and to a rodent sperm-coating glycoprotein (FEBS Lett. 380, 246-250, 1996). The primary structure and properties of helothermine, a peptide toxin that blocks ryanodine receptors is described in Biophys. J. 68:2280-2288(1995). As GliPR, Helothermine belongs to a family that groups mammalian SCP/TPX1; insects AG3/AG5; FUNGI SC7/SC14 and plants PR-1.

Based upon homology, FCTR7 protein and each homologous protein or peptide may share at least some activity.

Therapeutic uses:

FCTR7 protein has homology to trypsin inhibitors, Q91055 helothermine, tumor derived tyrpsin inhibitors, glioma pathogenesis-related protein, Q9Z0U6 LATE GESTATION LUNG PROTEIN 1, and to the Prosite family which groups mammalian SCP/TPX1;INSECTS AG3/AG5; FUNGI SC7/SC14 AND PLANTS PR-1 proteins. Therefore the FCTR7 protein disclosed in this invention could function like the proteins which it has homology to. These functions include tissue development *in vitro* and *in vivo*, and cancer pathogenesis.

Based the tissue expression pattern, the gene is implicated in diseases of tissues in which it is expressed. These diseases include but are not limited to:

- Glioma,
- cancer,
- lung diseases,
- gestation,
- male and female reproductive diseases,
- deafness,
- neurological disorders,
- gastric disorders, and
- pancreatic diseases like diabetes.

These materials are further useful in the generation of antibodies that bind immunospecifically to the novel FCTR7 substances for use in therapeutic or diagnostic methods.

These antibodies may be generated according to methods known in the art, using prediction from hydrophobicity charts, as described in the "Anti-FCTRX Antibodies" section below. In one embodiment, a contemplated FCTR7 epitope is from aa 40 to 120. In another embodiment, a FCTR7 epitope is from aa 130 to 170. In additional embodiments, FCTR7 epitopes are from aa 210 to 230, and from aa 240 to 280.

TABLE 8A: Summary Of Nucleic Acids And Proteins Of The Invention

Name	Tables	Clone; Description of Homolog	Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO
FCTR1	1A, 1B,	58092213.0.36 follistatin-like protein	1	2
FCTR2	2A, 2B	AC012614_1.0.123; KIAA1061-like protein	3	4
FCTR3	3A, 3B	10129612.0.118; neurestin-like protein	5	6
	3C, 3D	10129612.0.405; neurestin-like protein	7	8
	3E	10129612.0.154; neurestin-like protein	9	
	3F	10129612.0.67; neurestin-like protein	10	
	3G	10129612.0.258; neurestin-like protein	11	
	3H, 3I	10129612.0.352; neurestin-like protein	12	13
FCTR4	4A, 4B	29692275.0.1; NF-Kappa-B P65delta3-like protein	14	15
FCTR5	5A, 5B	32125243.0.21; human complement C1R component precursor -like protein	16	17
	5C, 5D		18	19
FCTR6	6A, 6B	27455183.0.19; novel human blood coagulation factor XI -like protein	20	21
	6C, 6D	27455183.0.145; novel human blood coagulation factor XI -like protein	22	23
FCTR7	7A, 7B	32592466.0.64; trypsin inhibitor -like protein	24	25
FCTR1	Example 2	Ag809 Forward	26	
FCTR1	Example 2	Ag809 Probe	27	
FCTR1	Example 2	Ag809 Reverse	28	
FCTR4	Example 2	Ag2773 Forward	29	
FCTR4	Example 2	Ag2773 Probe	30	
FCTR4	Example 2	Ag2773 Reverse	31	
FCTR5	Example 2	Ag427 Forward	32	
FCTR5	Example 2	Ag427 Probe	33	
FCTR5	Example 2	Ag427 Reverse	34	
FCTR6	Example 2	Ag1541 Forward	35	
FCTR6	Example 2	Ag1541 Probe	36	
FCTR6	Example 2	Ag1541 Reverse	37	

TABLE 8B: Summary of Query Sequences Disclosed

Table	Database	Acc. No.	Sequence Name	Species	SEQ ID NO.
1C, 1K	remtrEmbl	BAA21725	IGFBP-like protein	mouse	38
1D	sptrEmbl	Q61581	Follistatin-like protein-2	Mouse	39

1E	SptrEmbl	[redacted]7822	Mac25 protein	Human	40
1F, 1K	SptrEmbl	[redacted]812	Mac25 protein	Mouse	41
1G, 1K	SptrEmbl	Q16270	Prostacyclin-stimulating factor	Human	42
1H, 1K	PIR	B40098	Colorectal cancer suppressor	Rat	43
1I	TrEmblnew	AAD9360	PTP sigma (brain) precursor	Human	44
1J	SptrEmbl	Q13332	PTP sigma precursor	Human	45
2C	GenBank	AB028984	KIAA1061 cDNA	Human	46
2D	TrEmblnew	BAA85677	KIAA1263	Human	47
2E	TrEmblnew	BAA83013	KIAA1061 protein fragment	Human	48
2F	Embl	CAB70877.1	Hypothetical protein DKFzp566D234.1	Human	49
2G	GenBank	Q62632	Follistatin-related protein-1 precursor	Rat	50
2H	GenBank	Q62536	Follistatin-related protein-1 precursor	Mouse	51
2I	GenBank	JG0187	Follistatin related protein	African clawed frog	52
2J	GenBank	Q12841	Follistatin related protein-1 precursor	Human	53
2K	Embl	CAB42968.1	Flik protein	Chicken	54
2L	GenBank	T13822	Frazzled gene protein	Fruit fly	55
2M	GenBank	AAC38849.1	Roundabout 1	Fruit fly	56
2N	GenBank	O60469	Down Syndrome Cell Adhesion Molecule Precursor	Human`	57
2O	SwissProt	Q13449	Limbic system-associated membrane protein precursor	Human	58
2P	SptrEmbl	O70246	Putative neuronal cell adhesion molecule, short form	Mouse	59
2Q	SptrEmbl	O02869	CHLAMP, G11-isoform precursor	Chicken	60
2R	SwissProt	Q62813	Limbic system-associated membrane protein precursor	Rat	61
3J	GenBank	NM_011856.2	Odd Oz/ten-m homology 2	Fruit fly	62
3K	Embl	AJ245711.1	Teneurin-2 cDNA, short splice variant	Chicken	63
3L	GenBank	AB032953	KIAA 1127 cDNA	Human	64
3M, 3U	GenBank	AB025411	Ten-m2 cDNA	Mouse	65
3N	GenBank	NM_020088.1	Neurestin alpha cDNA	Rat	66
3O	Embl	GGA278031	Teneurin-2	Chicken	67
3P	GenBank	NP_035986.2	Odd Oz/ten-m homology 2	Fruit fly	68
3Q	Embl	CAC09416.1	Teneurin-2	Chicken	69
3R	GenBank	BAA77399.1	Ten-m4	Mouse	70
3S	GenBank	AB032953	KIAA1127 protein	Human	71
3T	GenBank	AF086607	Neurestin alpha	Rat	72
4C	SptrEmbl	Q99233	Hypothetical 10 kD protein	Trypanosome	73
4C	SptrEmbl	Q16896	GABA receptor subunit		74
4C	SptrEmbl	O76473	GABA receptor subunit		75
4C	TrEmblnew	AAD28317	FI3J11.13 protein		76

Text p. 90	SptrEmbl	[redacted]313	NF-kappa B P65 delta 3 pro[redacted]	Human	77
5E	GenBank	[redacted]_007061.1	Complement C1R-like prote[redacted]e precursor	Human	78
5F	GenBank	NM_001733.1	Complement component 1, R subcomponent cDNA	Human	79
5G	GenBank	AAF44349.1	Complement C1R-like proteinase precursor	Human	80
5H	GenBank	AAA5185.1	Complement C1R component precursor	Human	81
6E	GenBank	AB046651	Brain cDNA clone Qcc-17034	Macaque	82
6F	GenBank	AK09660	Adult testis cDNA, RIKEN full length enriched	Mouse	83
6G	GenBank	AB046651	Hypothetical protein	Macaque	84
6H	GenBank	NP_000838.1	Plasma kallikrein B1 precursor	Human	85
6I	GenBank	BAA37147.1	Kallikrein	Pig	86
6J	Embl	CAA64368.1	Coagulation factor XI	Human	87
7D, 7J	SptrEmbl	O43692	25 kDa trypsin inhibitor	Human	88
7D	SptrEmbl	O44228	HRTT-1		89
7D, 7K	SptrEmbl	P418060	Glioma pathogenesis-related protein	Human	90
7D	PIR-ID	JC4131	Glioma pathogenesis-related protein	Human	91
7D	SwissProt	O19010	Cysteine-rcih secretory protein		92
7E	GenBank	AF142573	Putatitive secretory protein precursor cDNA	Human	93
7F	GenBank	AF142573	Putative secretory protein precursor	Human	94
7G	GenBank	AF109674	Late gestation lung protein 1	Rat	95
7H	GenBank	D45027	R3H domain containing preprotein, 25 kDa trypsin inhibitor	Human	96
7I	Embl	AL117382	Novel protein similar to a trypsin inhibitor	Human	97
7L	PIR-ID	S68691	Neutrophil granules matrix glycoprotein SGP28 precursor	Human	98

FCTRX Nucleic Acids and Polypeptides

One aspect of the invention pertains to isolated nucleic acid molecules that encode FCTRX polypeptides or biologically-active portions thereof. Also included in the invention are nucleic acid fragments sufficient for use as hybridization probes to identify FCTRX-encoding nucleic acids (*e.g.*, FCTRX mRNAs) and fragments for use as PCR primers for the amplification and/or mutation of FCTRX nucleic acid molecules. As used herein, the term "nucleic acid molecule" is intended to include DNA molecules (*e.g.*, cDNA or genomic DNA), RNA molecules (*e.g.*, mRNA), analogs of the DNA or RNA generated using nucleotide analogs, and derivatives, fragments and homologs thereof. The nucleic acid molecule may be single-stranded or double-stranded, but preferably is comprised double-stranded DNA.

An FCTRX nucleic acid can encode a mature FCTRX polypeptide. As used herein, a "mature" form of a polypeptide or protein disclosed in the present invention is the product of a naturally occurring polypeptide or precursor form or proprotein. The naturally occurring polypeptide, precursor or proprotein includes, by way of nonlimiting example, the full length gene product, encoded by the corresponding gene. Alternatively, it may be defined as the polypeptide, precursor or proprotein encoded by an ORF described herein. The product "mature" form arises, again by way of nonlimiting example, as a result of one or more naturally occurring processing steps as they may take place within the cell, or host cell, in which the gene product arises. Examples of such processing steps leading to a "mature" form of a polypeptide or protein include the cleavage of the N-terminal methionine residue encoded by the initiation codon of an ORF, or the proteolytic cleavage of a signal peptide or leader sequence. Thus a mature form arising from a precursor polypeptide or protein that has residues 1 to N, where residue 1 is the N-terminal methionine, would have residues 2 through N remaining after removal of the N-terminal methionine. Alternatively, a mature form arising from a precursor polypeptide or protein having residues 1 to N, in which an N-terminal signal sequence from residue 1 to residue M is cleaved, would have the residues from residue M+1 to residue N remaining. Further as used herein, a "mature" form of a polypeptide or protein may arise from a step of post-translational modification other than a proteolytic cleavage event. Such additional processes include, by way of non-limiting example, glycosylation, myristoylation or phosphorylation. In general, a mature polypeptide or protein may result from the operation of only one of these processes, or a combination of any of them.

The term "probes", as utilized herein, refers to nucleic acid sequences of variable length, preferably between at least about 10 nucleotides (nt), 100 nt, or as many as approximately, *e.g.*, 6,000 nt, depending upon the specific use. Probes are used in the detection of identical, similar, or complementary nucleic acid sequences. Longer length probes are generally obtained from a natural or recombinant source, are highly specific, and much slower to hybridize than shorter-length oligomer probes. Probes may be single- or double-stranded and designed to have specificity in PCR, membrane-based hybridization technologies, or ELISA-like technologies.

The term "isolated" nucleic acid molecule, as utilized herein, is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid. Preferably, an "isolated" nucleic acid is free of sequences which naturally flank the nucleic acid (*i.e.*, sequences located at the 5'- and 3'-termini of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated FCTRX nucleic acid molecules can contain less than about 5 kb, 4 kb, 3 kb, 2 kb, 1 kb,

0.5 kb or 0.1 kb of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell or tissue from which the nucleic acid is derived (*e.g.*, brain, heart, liver, spleen, etc.). Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material or culture medium when produced by recombinant techniques, or of chemical precursors or other chemicals when chemically synthesized.

A nucleic acid molecule of the invention, *e.g.*, a nucleic acid molecule having the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a complement of this aforementioned nucleotide sequence, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or a portion of the nucleic acid sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24 as a hybridization probe, FCTRX molecules can be isolated using standard hybridization and cloning techniques (*e.g.*, as described in Sambrook, *et al.*, (eds.), MOLECULAR CLONING: A LABORATORY MANUAL 2nd Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989; and Ausubel, *et al.*, (eds.), CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, New York, NY, 1993.)

A nucleic acid of the invention can be amplified using cDNA, mRNA or alternatively, genomic DNA, as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid so amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore, oligonucleotides corresponding to FCTRX nucleotide sequences can be prepared by standard synthetic techniques, *e.g.*, using an automated DNA synthesizer.

As used herein, the term "oligonucleotide" refers to a series of linked nucleotide residues, which oligonucleotide has a sufficient number of nucleotide bases to be used in a PCR reaction. A short oligonucleotide sequence may be based on, or designed from, a genomic or cDNA sequence and is used to amplify, confirm, or reveal the presence of an identical, similar or complementary DNA or RNA in a particular cell or tissue. Oligonucleotides comprise portions of a nucleic acid sequence having about 10 nt, 50 nt, or 100 nt in length, preferably about 15 nt to 30 nt in length. In one embodiment of the invention, an oligonucleotide comprising a nucleic acid molecule less than 100 nt in length would further comprise at least 6 contiguous nucleotides of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a complement thereof. Oligonucleotides may be chemically synthesized and may also be used as probes.

In another embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule that is a complement of the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a portion of this nucleotide sequence (*e.g.*, a

fragment that can be used as a probe or primer or a fragment encoding a biologically-active portion of an FCTRX polypeptide). A nucleic acid molecule that is complementary to the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, is one that is sufficiently complementary to the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, that it can hydrogen bond with little or no mismatches to the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, thereby forming a stable duplex.

As used herein, the term "complementary" refers to Watson-Crick or Hoogsteen base pairing between nucleotides units of a nucleic acid molecule, and the term "binding" means the physical or chemical interaction between two polypeptides or compounds or associated polypeptides or compounds or combinations thereof. Binding includes ionic, non-ionic, van der Waals, hydrophobic interactions, and the like. A physical interaction can be either direct or indirect. Indirect interactions may be through or due to the effects of another polypeptide or compound. Direct binding refers to interactions that do not take place through, or due to, the effect of another polypeptide or compound, but instead are without other substantial chemical intermediates.

Fragments provided herein are defined as sequences of at least 6 (contiguous) nucleic acids or at least 4 (contiguous) amino acids, a length sufficient to allow for specific hybridization in the case of nucleic acids or for specific recognition of an epitope in the case of amino acids, respectively, and are at most some portion less than a full length sequence. Fragments may be derived from any contiguous portion of a nucleic acid or amino acid sequence of choice. Derivatives are nucleic acid sequences or amino acid sequences formed from the native compounds either directly or by modification or partial substitution. Analogs are nucleic acid sequences or amino acid sequences that have a structure similar to, but not identical to, the native compound but differs from it in respect to certain components or side chains. Analogs may be synthetic or from a different evolutionary origin and may have a similar or opposite metabolic activity compared to wild type. Homologs are nucleic acid sequences or amino acid sequences of a particular gene that are derived from different species.

Derivatives and analogs may be full length or other than full length, if the derivative or analog contains a modified nucleic acid or amino acid, as described below. Derivatives or analogs of the nucleic acids or proteins of the invention include, but are not limited to, molecules comprising regions that are substantially homologous to the nucleic acids or proteins of the invention, in various embodiments, by at least about 70%, 80%, or 95% identity (with a preferred identity of 80-95%) over a nucleic acid or amino acid sequence of identical size or

when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art, or whose encoding nucleic acid is capable of hybridizing to the complement of a sequence encoding the aforementioned proteins under stringent, moderately stringent, or low stringent conditions. See *e.g.* Ausubel, *et al.*, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, New York, NY, 1993, and below.

A "homologous nucleic acid sequence" or "homologous amino acid sequence," or variations thereof, refer to sequences characterized by a homology at the nucleotide level or amino acid level as discussed above. Homologous nucleotide sequences encode those sequences coding for isoforms of FCTRX polypeptides. Isoforms can be expressed in different tissues of the same organism as a result of, for example, alternative splicing of RNA. Alternatively, isoforms can be encoded by different genes. In the invention, homologous nucleotide sequences include nucleotide sequences encoding for an FCTRX polypeptide of species other than humans, including, but not limited to: vertebrates, and thus can include, *e.g.*, frog, mouse, rat, rabbit, dog, cat cow, horse, and other organisms. Homologous nucleotide sequences also include, but are not limited to, naturally occurring allelic variations and mutations of the nucleotide sequences set forth herein. A homologous nucleotide sequence does not, however, include the exact nucleotide sequence encoding human FCTRX protein. Homologous nucleic acid sequences include those nucleic acid sequences that encode conservative amino acid substitutions (see below) in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, as well as a polypeptide possessing FCTRX biological activity. Various biological activities of the FCTRX proteins are described below.

An FCTRX polypeptide is encoded by the open reading frame ("ORF") of an FCTRX nucleic acid. An ORF corresponds to a nucleotide sequence that could potentially be translated into a polypeptide. A stretch of nucleic acids comprising an ORF is uninterrupted by a stop codon. An ORF that represents the coding sequence for a full protein begins with an ATG "start" codon and terminates with one of the three "stop" codons, namely, TAA, TAG, or TGA. For the purposes of this invention, an ORF may be any part of a coding sequence, with or without a start codon, a stop codon, or both. For an ORF to be considered as a good candidate for coding for a *bona fide* cellular protein, a minimum size requirement is often set, *e.g.*, a stretch of DNA that would encode a protein of 50 amino acids or more.

The nucleotide sequences determined from the cloning of the human FCTRX genes allows for the generation of probes and primers designed for use in identifying and/or cloning FCTRX homologues in other cell types, *e.g.* from other tissues, as well as FCTRX homologues from other vertebrates. The probe/primer typically comprises substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that

hybridizes under stringent conditions to at least about 12, 25, 50, 100, 150, 200, 250, 300, 350 or 400 consecutive sense strand nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24; or an anti-sense strand nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24; or of a naturally occurring mutant of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24.

Probes based on the human FCTRX nucleotide sequences can be used to detect transcripts or genomic sequences encoding the same or homologous proteins. In various embodiments, the probe further comprises a label group attached thereto, *e.g.* the label group can be a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes can be used as a part of a diagnostic test kit for identifying cells or tissues which mis-express an FCTRX protein, such as by measuring a level of an FCTRX-encoding nucleic acid in a sample of cells from a subject *e.g.*, detecting FCTRX mRNA levels or determining whether a genomic FCTRX gene has been mutated or deleted.

"A polypeptide having a biologically-active portion of an FCTRX polypeptide" refers to polypeptides exhibiting activity similar, but not necessarily identical to, an activity of a polypeptide of the invention, including mature forms, as measured in a particular biological assay, with or without dose dependency. A nucleic acid fragment encoding a "biologically-active portion of FCTRX" can be prepared by isolating a portion of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, that encodes a polypeptide having an FCTRX biological activity (the biological activities of the FCTRX proteins are described below), expressing the encoded portion of FCTRX protein (*e.g.*, by recombinant expression *in vitro*) and assessing the activity of the encoded portion of FCTRX.

FCTRX Nucleic Acid and Polypeptide Variants

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequences shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, due to degeneracy of the genetic code and thus encode the same FCTRX proteins as that encoded by the nucleotide sequences shown in SEQ ID NO NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24. In another embodiment, an isolated nucleic acid molecule of the invention has a nucleotide sequence encoding a protein having an amino acid sequence shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25.

In addition to the human FCTRX nucleotide sequences shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, it will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of the FCTRX

polypeptides may exist within a population (*e.g.*, the human population). Such genetic polymorphism in the FCTRX genes may exist among individuals within a population due to natural allelic variation. As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame (ORF) encoding an FCTRX protein, preferably a vertebrate FCTRX protein. Such natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of the FCTRX genes. Any and all such nucleotide variations and resulting amino acid polymorphisms in the FCTRX polypeptides, which are the result of natural allelic variation and that do not alter the functional activity of the FCTRX polypeptides, are intended to be within the scope of the invention.

Moreover, nucleic acid molecules encoding FCTRX proteins from other species, and thus that have a nucleotide sequence that differs from the human sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, are intended to be within the scope of the invention. Nucleic acid molecules corresponding to natural allelic variants and homologues of the FCTRX cDNAs of the invention can be isolated based on their homology to the human FCTRX nucleic acids disclosed herein using the human cDNAs, or a portion thereof, as a hybridization probe according to standard hybridization techniques under stringent hybridization conditions.

Accordingly, in another embodiment, an isolated nucleic acid molecule of the invention is at least 6 nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24. In another embodiment, the nucleic acid is at least 10, 25, 50, 100, 250, 500, 750, 1000, 1500, or 2000 or more nucleotides in length. In yet another embodiment, an isolated nucleic acid molecule of the invention hybridizes to the coding region. As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 60% homologous to each other typically remain hybridized to each other.

Homologs (*i.e.,* nucleic acids encoding FCTRX proteins derived from species other than human) or other related sequences (*e.g.,* paralogs) can be obtained by low, moderate or high stringency hybridization with all or a portion of the particular human sequence as a probe using methods well known in the art for nucleic acid hybridization and cloning.

As used herein, the phrase "stringent hybridization conditions" refers to conditions under which a probe, primer or oligonucleotide will hybridize to its target sequence, but to no other sequences. Stringent conditions are sequence-dependent and will be different in different circumstances. Longer sequences hybridize specifically at higher temperatures than shorter sequences. Generally, stringent conditions are selected to be about 5°C lower than the thermal

melting point (Tm) for the specific sequence at a defined ionic strength and pH. The Tm is the temperature (under defined ionic strength, pH and nucleic acid concentration) at which 50% of the probes complementary to the target sequence hybridize to the target sequence at equilibrium. Since the target sequences are generally present at excess, at Tm, 50% of the probes are occupied at equilibrium. Typically, stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M sodium ion (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30°C for short probes, primers or oligonucleotides (*e.g.*, 10 nt to 50 nt) and at least about 60°C for longer probes, primers and oligonucleotides. Stringent conditions may also be achieved with the addition of destabilizing agents, such as formamide.

Stringent conditions are known to those skilled in the art and can be found in Ausubel, *et al.*, (eds.), CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. Preferably, the conditions are such that sequences at least about 65%, 70%, 75%, 85%, 90%, 95%, 98%, or 99% homologous to each other typically remain hybridized to each other. A non-limiting example of stringent hybridization conditions are hybridization in a high salt buffer comprising 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 mg/ml denatured salmon sperm DNA at 65°C, followed by one or more washes in 0.2X SSC, 0.01% BSA at 50°C. An isolated nucleic acid molecule of the invention that hybridizes under stringent conditions to the sequences of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, corresponds to a naturally-occurring nucleic acid molecule. As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (*e.g.*, encodes a natural protein).

In a second embodiment, a nucleic acid sequence that is hybridizable to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments, analogs or derivatives thereof, under conditions of moderate stringency is provided. A non-limiting example of moderate stringency hybridization conditions are hybridization in 6X SSC, 5X Denhardt's solution, 0.5% SDS and 100 mg/ml denatured salmon sperm DNA at 55°C, followed by one or more washes in 1X SSC, 0.1% SDS at 37°C. Other conditions of moderate stringency that may be used are well-known within the art. See, *e.g.*, Ausubel, et *al.* (eds.), 1993, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, NY, and Kriegler, 1990; GENE TRANSFER AND EXPRESSION, A LABORATORY MANUAL, Stockton Press, NY.

In a third embodiment, a nucleic acid that is hybridizable to the nucleic acid molecule comprising the nucleotide sequences of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments, analogs or derivatives thereof, under conditions of low stringency, is provided. A non-limiting example of low stringency hybridization conditions are hybridization in 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 mg/ml denatured salmon sperm DNA, 10% (wt/vol) dextran sulfate at 40°C, followed by one or more washes in 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS at 50°C. Other conditions of low stringency that may be used are well known in the art (*e.g.*, as employed for cross-species hybridizations). See, *e.g.,* Ausubel, *et al.* (eds.), 1993, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, NY, and Kriegler, 1990, GENE TRANSFER AND EXPRESSION, A LABORATORY MANUAL, Stockton Press, NY; Shilo and Weinberg, 1981. *Proc Natl Acad Sci USA* **78**: 6789-6792.

Conservative Mutations

In addition to naturally-occurring allelic variants of FCTRX sequences that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequences of SEQ ID NO NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, thereby leading to changes in the amino acid sequences of the encoded FCTRX proteins, without altering the functional ability of said FCTRX proteins. For example, nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues can be made in the sequence of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequences of the FCTRX proteins without altering their biological activity, whereas an "essential" amino acid residue is required for such biological activity. For example, amino acid residues that are conserved among the FCTRX proteins of the invention are predicted to be particularly non-amenable to alteration. Amino acids for which conservative substitutions can be made are well-known within the art.

Another aspect of the invention pertains to nucleic acid molecules encoding FCTRX proteins that contain changes in amino acid residues that are not essential for activity. Such FCTRX proteins differ in amino acid sequence from SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, yet retain biological activity. In one embodiment, the isolated nucleic acid molecule comprises a nucleotide sequence encoding a protein, wherein the protein comprises an amino acid sequence at least about 45% homologous to the amino acid sequences of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. Preferably, the protein encoded by the nucleic acid molecule is at least about 60% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; more

preferably at least about 70% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; still more preferably at least about 80% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; even more preferably at least about 90% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; and most preferably at least about 95% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25.

An isolated nucleic acid molecule encoding an FCTRX protein homologous to the protein of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein.

Mutations can be introduced into SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted, non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined within the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted non-essential amino acid residue in the FCTRX protein is replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of an FCTRX coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for FCTRX biological activity to identify mutants that retain activity. Following mutagenesis of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, the encoded protein can be expressed by any recombinant technology known in the art and the activity of the protein can be determined.

The relatedness of amino acid families may also be determined based on side chain interactions. Substituted amino acids may be fully conserved "strong" residues or fully conserved "weak" residues. The "strong" group of conserved amino acid residues may be any one of the following groups: STA, NEQK, NHQK, NDEQ, QHRK, MILV, MILF, HY, FYW, wherein the single letter amino acid codes are grouped by those amino acids that may be substituted for each other. Likewise, the "weak" group of conserved residues may be any one of

the following: CSA, ATV, SAG, STNK, STPA, SGND, SNDEQ, NDEQHK, NEQHRK, VLIM, HFY, wherein the letters within each group represent the single letter amino acid code.

In one embodiment, a mutant FCTRX protein can be assayed for (*i*) the ability to form protein:protein interactions with other FCTRX proteins, other cell-surface proteins, or biologically-active portions thereof, (*ii*) complex formation between a mutant FCTRX protein and an FCTRX ligand; or (*iii*) the ability of a mutant FCTRX protein to bind to an intracellular target protein or biologically-active portion thereof; (*e.g.* avidin proteins).

In yet another embodiment, a mutant FCTRX protein can be assayed for the ability to regulate a specific biological function (*e.g.*, regulation of insulin release).

Antisense Nucleic Acids

Another aspect of the invention pertains to isolated antisense nucleic acid molecules that are hybridizable to or complementary to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments, analogs or derivatives thereof. An "antisense" nucleic acid comprises a nucleotide sequence that is complementary to a "sense" nucleic acid encoding a protein (*e.g.*, complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence). In specific aspects, antisense nucleic acid molecules are provided that comprise a sequence complementary to at least about 10, 25, 50, 100, 250 or 500 nucleotides or an entire FCTRX coding strand, or to only a portion thereof. Nucleic acid molecules encoding fragments, homologs, derivatives and analogs of an FCTRX protein of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; or antisense nucleic acids complementary to an FCTRX nucleic acid sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, are additionally provided.

In one embodiment, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a nucleotide sequence encoding an FCTRX protein. The term "coding region" refers to the region of the nucleotide sequence comprising codons which are translated into amino acid residues. In another embodiment, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence encoding the FCTRX protein. The term "noncoding region" refers to 5' and 3' sequences which flank the coding region that are not translated into amino acids (*i.e.*, also referred to as 5' and 3' untranslated regions).

Given the coding strand sequences encoding the FCTRX protein disclosed herein, antisense nucleic acids of the invention can be designed according to the rules of Watson and

Crick or Hoogsteen base-pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of FCTRX mRNA, but more preferably is an oligonucleotide that is antisense to only a portion of the coding or noncoding region of FCTRX mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of FCTRX mRNA. An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis or enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (*e.g.*, an antisense oligonucleotide) can be chemically synthesized using naturally-occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids (*e.g.*, phosphorothioate derivatives and acridine substituted nucleotides can be used).

Examples of modified nucleotides that can be used to generate the antisense nucleic acid include: 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (*i.e.*, RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding an FCTRX protein to thereby inhibit expression of the protein (*e.g.*, by inhibiting transcription and/or translation). The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule that binds to DNA duplexes, through specific interactions in the major groove of the

double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface (*e.g.*, by linking the antisense nucleic acid molecules to peptides or antibodies that bind to cell surface receptors or antigens). The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient nucleic acid molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

In yet another embodiment, the antisense nucleic acid molecule of the invention is an α-anomeric nucleic acid molecule. An α-anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β-units, the strands run parallel to each other. See, *e.g.,* Gaultier, *et al.*, 1987. *Nucl. Acids Res.* **15**: 6625-6641. The antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (see, *e.g.,* Inoue, *et al.* 1987. *Nucl. Acids Res.* **15**: 6131-6148) or a chimeric RNA-DNA analogue (see, *e.g.,* Inoue, *et al.*, 1987. *FEBS Lett.* **215**: 327-330.

Ribozymes and PNA Moieties

Nucleic acid modifications include, by way of non-limiting example, modified bases, and nucleic acids whose sugar phosphate backbones are modified or derivatized. These modifications are carried out at least in part to enhance the chemical stability of the modified nucleic acid, such that they may be used, for example, as antisense binding nucleic acids in therapeutic applications in a subject.

In one embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity that are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes as described in Haselhoff and Gerlach 1988. *Nature* 334: 585-591) can be used to catalytically cleave FCTRX mRNA transcripts to thereby inhibit translation of FCTRX mRNA. A ribozyme having specificity for an FCTRX-encoding nucleic acid can be designed based upon the nucleotide sequence of an FCTRX cDNA disclosed herein (*i.e.*, SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24). For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in an FCTRX-encoding mRNA. See, *e.g.*, U.S. Patent 4,987,071 to Cech, *et al.* and U.S. Patent

5,116,742 to Cech, *et al.* FCTRX mRNA can also be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, *e.g.*, Bartel *et al.*, (1993) *Science* 261:1411-1418.

Alternatively, FCTRX gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region of the FCTRX nucleic acid (*e.g.*, the FCTRX promoter and/or enhancers) to form triple helical structures that prevent transcription of the FCTRX gene in target cells. *See, e.g.,* Helene, 1991. *Anticancer Drug Des.* 6: 569-84; Helene, *et al.* 1992. *Ann. N.Y. Acad. Sci.* 660: 27-36; Maher, 1992. *Bioassays* 14: 807-15.

In various embodiments, the FCTRX nucleic acids can be modified at the base moiety, sugar moiety or phosphate backbone to improve, *e.g.*, the stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate peptide nucleic acids. *See, e.g.,* Hyrup, *et al.*, 1996. *Bioorg Med Chem* 4: 5-23. As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics (*e.g.*, DNA mimics) in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup, *et al.*, 1996. *supra*; Perry-O'Keefe, *et al.*, 1996. *Proc. Natl. Acad. Sci. USA* 93: 14670-14675.

PNAs of FCTRX can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, *e.g.*, inducing transcription or translation arrest or inhibiting replication. PNAs of FCTRX can also be used, for example, in the analysis of single base pair mutations in a gene (*e.g.*, PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, *e.g.*, S_1 nucleases (*see,* Hyrup, *et al.,* 1996.*supra*); or as probes or primers for DNA sequence and hybridization (*see,* Hyrup, *et al.*, 1996, *supra*; Perry-O'Keefe, *et al.,* 1996. *supra*).

In another embodiment, PNAs of FCTRX can be modified, *e.g.*, to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras of FCTRX can be generated that may combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes (*e.g.*, RNase H and DNA polymerases) to interact with the DNA portion while the PNA portion would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using

linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation (*see,* Hyrup, etal., 1996. *supra*). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup, *et al.,* 1996. *supra* and Finn, *et al.*, 1996. *Nucl Acids Res* 24: 3357-3363. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry, and modified nucleoside analogs, *e.g.*, 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite, can be used between the PNA and the 5' end of DNA. *See, e.g.,* Mag, *et al.*, 1989. *Nucl Acid Res* 17: 5973-5988. PNA monomers are then coupled in a stepwise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment. *See, e.g.,* Finn, *et al.*, 1996. *supra*. Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment. *See, e.g.,* Petersen, *et al.*, 1975. *Bioorg. Med. Chem. Lett.* 5: 1119-11124.

In other embodiments, the oligonucleotide may include other appended groups such as peptides (*e.g.*, for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (*see, e.g.*, Letsinger, *et al.*, 1989. *Proc. Natl. Acad. Sci. U.S.A.* 86: 6553-6556; Lemaitre, *et al.*, 1987. *Proc. Natl. Acad. Sci.* 84: 648-652; PCT Publication No. WO88/09810) or the blood-brain barrier (*see, e.g.*, PCT Publication No. WO 89/10134). In addition, oligonucleotides can be modified with hybridization triggered cleavage agents (*see, e.g.,* Krol, *et al.*, 1988. *BioTechniques* 6:958-976) or intercalating agents (*see, e.g.*, Zon, 1988. *Pharm. Res.* 5: 539-549). To this end, the oligonucleotide may be conjugated to another molecule, *e.g.*, a peptide, a hybridization triggered cross-linking agent, a transport agent, a hybridization-triggered cleavage agent, and the like.

FCTRX Polypeptides

A polypeptide according to the invention includes a polypeptide including the amino acid sequence of FCTRX polypeptides whose sequences are provided in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. The invention also includes a mutant or variant protein any of whose residues may be changed from the corresponding residues shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, while still encoding a protein that maintains its FCTRX activities and physiological functions, or a functional fragment thereof.

In general, an FCTRX variant that preserves FCTRX-like function includes any variant in which residues at a particular position in the sequence have been substituted by other amino acids, and further include the possibility of inserting an additional residue or residues between two residues of the parent protein as well as the possibility of deleting one or more residues from the parent sequence. Any amino acid substitution, insertion, or deletion is encompassed by the

invention. In favorable circumstances, the substitution is a conservative substitution as defined above.

One aspect of the invention pertains to isolated FCTRX proteins, and biologically-active portions thereof, or derivatives, fragments, analogs or homologs thereof. Also provided are polypeptide fragments suitable for use as immunogens to raise anti-FCTRX antibodies. In one embodiment, native FCTRX proteins can be isolated from cells or tissue sources by an appropriate purification scheme using standard protein purification techniques. In another embodiment, FCTRX proteins are produced by recombinant DNA techniques. Alternative to recombinant expression, an FCTRX protein or polypeptide can be synthesized chemically using standard peptide synthesis techniques.

An "isolated" or "purified" polypeptide or protein or biologically-active portion thereof is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the FCTRX protein is derived, or substantially free from chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of FCTRX proteins in which the protein is separated from cellular components of the cells from which it is isolated or recombinantly-produced. In one embodiment, the language "substantially free of cellular material" includes preparations of FCTRX proteins having less than about 30% (by dry weight) of non-FCTRX proteins (also referred to herein as a "contaminating protein"), more preferably less than about 20% of non-FCTRX proteins, still more preferably less than about 10% of non-FCTRX proteins, and most preferably less than about 5% of non-FCTRX proteins. When the FCTRX protein or biologically-active portion thereof is recombinantly-produced, it is also preferably substantially free of culture medium, *i.e.*, culture medium represents less than about 20%, more preferably less than about 10%, and most preferably less than about 5% of the volume of the FCTRX protein preparation.

The language "substantially free of chemical precursors or other chemicals" includes preparations of FCTRX proteins in which the protein is separated from chemical precursors or other chemicals that are involved in the synthesis of the protein. In one embodiment, the language "substantially free of chemical precursors or other chemicals" includes preparations of FCTRX proteins having less than about 30% (by dry weight) of chemical precursors or non-FCTRX chemicals, more preferably less than about 20% chemical precursors or non-FCTRX chemicals, still more preferably less than about 10% chemical precursors or non-FCTRX chemicals, and most preferably less than about 5% chemical precursors or non-FCTRX chemicals.

Biologically-active portions of FCTRX proteins include peptides comprising amino acid sequences sufficiently homologous to or derived from the amino acid sequences of the FCTRX proteins (*e.g.*, the amino acid sequence shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25) that include fewer amino acids than the full-length FCTRX proteins, and exhibit at least one activity of an FCTRX protein. Typically, biologically-active portions comprise a domain or motif with at least one activity of the FCTRX protein. A biologically-active portion of an FCTRX protein can be a polypeptide which is, for example, 10, 25, 50, 100 or more amino acid residues in length.

Moreover, other biologically-active portions, in which other regions of the protein are deleted, can be prepared by recombinant techniques and evaluated for one or more of the functional activities of a native FCTRX protein.

In an embodiment, the FCTRX protein has an amino acid sequence shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. In other embodiments, the FCTRX protein is substantially homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, and retains the functional activity of the protein of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, yet differs in amino acid sequence due to natural allelic variation or mutagenesis, as described in detail, below. Accordingly, in another embodiment, the FCTRX protein is a protein that comprises an amino acid sequence at least about 45% homologous to the amino acid sequence of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, and retains the functional activity of the FCTRX proteins of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25.

Determining Homology Between Two or More Sequences

To determine the percent homology of two amino acid sequences or of two nucleic acids, the sequences are aligned for optimal comparison purposes (*e.g.*, gaps can be introduced in the sequence of a first amino acid or nucleic acid sequence for optimal alignment with a second amino or nucleic acid sequence). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are homologous at that position (*i.e.*, as used herein amino acid or nucleic acid "homology" is equivalent to amino acid or nucleic acid "identity").

The nucleic acid sequence homology may be determined as the degree of identity between two sequences. The homology may be determined using computer programs known in the art, such as GAP software provided in the GCG program package. *See,* Needleman and Wunsch, 1970. *J Mol Biol* 48: 443-453. Using GCG GAP software with the following settings for nucleic acid sequence comparison: GAP creation penalty of 5.0 and GAP extension penalty

of 0.3, the coding region of the analogous nucleic acid sequences referred to above exhibits a degree of identity preferably of at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99%, with the CDS (encoding) part of the DNA sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24.

The term "sequence identity" refers to the degree to which two polynucleotide or polypeptide sequences are identical on a residue-by-residue basis over a particular region of comparison. The term "percentage of sequence identity" is calculated by comparing two optimally aligned sequences over that region of comparison, determining the number of positions at which the identical nucleic acid base (*e.g.*, A, T, C, G, U, or I, in the case of nucleic acids) occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the region of comparison (*i.e.*, the window size), and multiplying the result by 100 to yield the percentage of sequence identity. The term "substantial identity" as used herein denotes a characteristic of a polynucleotide sequence, wherein the polynucleotide comprises a sequence that has at least 80 percent sequence identity, preferably at least 85 percent identity and often 90 to 95 percent sequence identity, more usually at least 99 percent sequence identity as compared to a reference sequence over a comparison region.

Chimeric and Fusion Proteins

The invention also provides FCTRX chimeric or fusion proteins. As used herein, an FCTRX "chimeric protein" or "fusion protein" comprises an FCTRX polypeptide operatively-linked to a non-FCTRX polypeptide. An "FCTRX polypeptide" refers to a polypeptide having an amino acid sequence corresponding to an FCTRX protein (SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25), whereas a "non-FCTRX polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a protein that is not substantially homologous to the FCTRX protein, *e.g.*, a protein that is different from the FCTRX protein and that is derived from the same or a different organism. Within an FCTRX fusion protein the FCTRX polypeptide can correspond to all or a portion of an FCTRX protein. In one embodiment, an FCTRX fusion protein comprises at least one biologically-active portion of an FCTRX protein. In another embodiment, an FCTRX fusion protein comprises at least two biologically-active portions of an FCTRX protein. In yet another embodiment, an FCTRX fusion protein comprises at least three biologically-active portions of an FCTRX protein. Within the fusion protein, the term "operatively-linked" is intended to indicate that the FCTRX polypeptide and the non-FCTRX polypeptide are fused in-frame with one another. The non-FCTRX polypeptide can be fused to the N-terminus or C-terminus of the FCTRX polypeptide.

In one embodiment, the fusion protein is a GST-FCTRX fusion protein in which the FCTRX sequences are fused to the C-terminus of the GST (glutathione S-transferase) sequences. Such fusion proteins can facilitate the purification of recombinant FCTRX polypeptides.

In another embodiment, the fusion protein is an FCTRX protein containing a heterologous signal sequence at its N-terminus. In certain host cells (*e.g.*, mammalian host cells), expression and/or secretion of FCTRX can be increased through use of a heterologous signal sequence.

In yet another embodiment, the fusion protein is an FCTRX-immunoglobulin fusion protein in which the FCTRX sequences are fused to sequences derived from a member of the immunoglobulin protein family. The FCTRX-immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction between an FCTRX ligand and an FCTRX protein on the surface of a cell, to thereby suppress FCTRX-mediated signal transduction *in vivo*. The FCTRX-immunoglobulin fusion proteins can be used to affect the bioavailability of an FCTRX cognate ligand. Inhibition of the FCTRX ligand/FCTRX interaction may be useful therapeutically for both the treatment of proliferative and differentiative disorders, as well as modulating (*e.g.* promoting or inhibiting) cell survival. Moreover, the FCTRX-immunoglobulin fusion proteins of the invention can be used as immunogens to produce anti-FCTRX antibodies in a subject, to purify FCTRX ligands, and in screening assays to identify molecules that inhibit the interaction of FCTRX with an FCTRX ligand.

An FCTRX chimeric or fusion protein of the invention can be produced by standard recombinant DNA techniques. For example, DNA fragments coding for the different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, *e.g.*, by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers that give rise to complementary overhangs between two consecutive gene fragments that can subsequently be annealed and reamplified to generate a chimeric gene sequence (*see, e.g.,* Ausubel, *et al.* (eds.) CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (*e.g.*, a GST polypeptide). An FCTRX-encoding nucleic acid

can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the FCTRX protein.

FCTRX Agonists and Antagonists

The invention also pertains to variants of the FCTRX proteins that function as either FCTRX agonists (*i.e.*, mimetics) or as FCTRX antagonists. Variants of the FCTRX protein can be generated by mutagenesis (*e.g.*, discrete point mutation or truncation of the FCTRX protein). An agonist of the FCTRX protein can retain substantially the same, or a subset of, the biological activities of the naturally occurring form of the FCTRX protein. An antagonist of the FCTRX protein can inhibit one or more of the activities of the naturally occurring form of the FCTRX protein by, for example, competitively binding to a downstream or upstream member of a cellular signaling cascade which includes the FCTRX protein. Thus, specific biological effects can be elicited by treatment with a variant of limited function. In one embodiment, treatment of a subject with a variant having a subset of the biological activities of the naturally occurring form of the protein has fewer side effects in a subject relative to treatment with the naturally occurring form of the FCTRX proteins.

Variants of the FCTRX proteins that function as either FCTRX agonists (*i.e.*, mimetics) or as FCTRX antagonists can be identified by screening combinatorial libraries of mutants (*e.g.*, truncation mutants) of the FCTRX proteins for FCTRX protein agonist or antagonist activity. In one embodiment, a variegated library of FCTRX variants is generated by combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A variegated library of FCTRX variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a degenerate set of potential FCTRX sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (*e.g.*, for phage display) containing the set of FCTRX sequences therein. There are a variety of methods which can be used to produce libraries of potential FCTRX variants from a degenerate oligonucleotide sequence. Chemical synthesis of a degenerate gene sequence can be performed in an automatic DNA synthesizer, and the synthetic gene then ligated into an appropriate expression vector. Use of a degenerate set of genes allows for the provision, in one mixture, of all of the sequences encoding the desired set of potential FCTRX sequences. Methods for synthesizing degenerate oligonucleotides are well-known within the art. *See, e.g.*, Narang, 1983. *Tetrahedron* 39: 3; Itakura, *et al.*, 1984. *Annu. Rev. Biochem.* 53: 323; Itakura, *et al.*, 1984. *Science* 198: 1056; Ike, *et al.*, 1983. *Nucl. Acids Res.* 11: 477.

Polypeptide Libraries

In addition, libraries of fragments of the FCTRX protein coding sequences can be used to generate a variegated population of FCTRX fragments for screening and subsequent selection of variants of an FCTRX protein. In one embodiment, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of an FCTRX coding sequence with a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double-stranded DNA that can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed duplexes by treatment with S_1 nuclease, and ligating the resulting fragment library into an expression vector. By this method, expression libraries can be derived which encodes N-terminal and internal fragments of various sizes of the FCTRX proteins.

Various techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA libraries for gene products having a selected property. Such techniques are adaptable for rapid screening of the gene libraries generated by the combinatorial mutagenesis of FCTRX proteins. The most widely used techniques, which are amenable to high throughput analysis, for screening large gene libraries typically include cloning the gene library into replicable expression vectors, transforming appropriate cells with the resulting library of vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates isolation of the vector encoding the gene whose product was detected. Recursive ensemble mutagenesis (REM), a new technique that enhances the frequency of functional mutants in the libraries, can be used in combination with the screening assays to identify FCTRX variants. *See, e.g.,* Arkin and Yourvan, 1992. *Proc. Natl. Acad. Sci. USA* 89: 7811-7815; Delgrave, *et al.*, 1993. *Protein Engineering* 6:327-331.

Anti-FCTRX Antibodies

The invention encompasses antibodies and antibody fragments, such as F_{ab} or $(F_{ab})_2$, that bind immunospecifically to any of the FCTRX polypeptides of said invention.

An isolated FCTRX protein, or a portion or fragment thereof, can be used as an immunogen to generate antibodies that bind to FCTRX polypeptides using standard techniques for polyclonal and monoclonal antibody preparation. The full-length FCTRX proteins can be used or, alternatively, the invention provides antigenic peptide fragments of FCTRX proteins for use as immunogens. The antigenic FCTRX peptides comprises at least 4 amino acid residues of the amino acid sequence shown in SEQ ID NO NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, and

encompasses an epitope of FCTRX such that an antibody raised against the peptide forms a specific immune complex with FCTRX. Preferably, the antigenic peptide comprises at least 6, 8, 10, 15, 20, or 30 amino acid residues. Longer antigenic peptides are sometimes preferable over shorter antigenic peptides, depending on use and according to methods well known to someone skilled in the art.

In certain embodiments of the invention, at least one epitope encompassed by the antigenic peptide is a region of FCTRX that is located on the surface of the protein (*e.g.*, a hydrophilic region). As a means for targeting antibody production, hydropathy plots showing regions of hydrophilicity and hydrophobicity may be generated by any method well known in the art, including, for example, the Kyte Doolittle or the Hopp Woods methods, either with or without Fourier transformation (*see, e.g.*, Hopp and Woods, 1981. *Proc. Nat. Acad. Sci. USA* 78: 3824-3828; Kyte and Doolittle, 1982. *J. Mol. Biol.* 157: 105-142, each incorporated herein by reference in their entirety).

As disclosed herein, FCTRX protein sequences of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, or derivatives, fragments, analogs or homologs thereof, may be utilized as immunogens in the generation of antibodies that immunospecifically-bind these protein components. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically-active portions of immunoglobulin molecules, *i.e.*, molecules that contain an antigen binding site that specifically-binds (immunoreacts with) an antigen, such as FCTRX. Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, F_{ab} and $F_{(ab')2}$ fragments, and an F_{ab} expression library. In a specific embodiment, antibodies to human FCTRX proteins are disclosed. Various procedures known within the art may be used for the production of polyclonal or monoclonal antibodies to an FCTRX protein sequence of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, or a derivative, fragment, analog or homolog thereof. Some of these proteins are discussed below.

For the production of polyclonal antibodies, various suitable host animals (*e.g.*, rabbit, goat, mouse or other mammal) may be immunized by injection with the native protein, or a synthetic variant thereof, or a derivative of the foregoing. An appropriate immunogenic preparation can contain, for example, recombinantly-expressed FCTRX protein or a chemically-synthesized FCTRX polypeptide. The preparation can further include an adjuvant. Various adjuvants used to increase the immunological response include, but are not limited to, Freund's (complete and incomplete), mineral gels (*e.g.*, aluminum hydroxide), surface active substances (*e.g.*, lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, dinitrophenol, etc.), human adjuvants such as *Bacille Calmette-Guerin* and *Corynebacterium parvum*, or similar

immunostimulatory agents. If desired, the antibody molecules directed against FCTRX can be isolated from the mammal (*e.g.*, from the blood) and further purified by well known techniques, such as protein A chromatography to obtain the IgG fraction.

The term "monoclonal antibody" or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one species of an antigen binding site capable of immunoreacting with a particular epitope of FCTRX. A monoclonal antibody composition thus typically displays a single binding affinity for a particular FCTRX protein with which it immunoreacts. For preparation of monoclonal antibodies directed towards a particular FCTRX protein, or derivatives, fragments, analogs or homologs thereof, any technique that provides for the production of antibody molecules by continuous cell line culture may be utilized. Such techniques include, but are not limited to, the hybridoma technique (*see, e.g.,* Kohler & Milstein, 1975. *Nature* 256: 495-497); the trioma technique; the human B-cell hybridoma technique (*see, e.g.,* Kozbor, *et al.,* 1983. *Immunol. Today* 4: 72) and the EBV hybridoma technique to produce human monoclonal antibodies (*see, e.g.,* Cole, *et al.,* 1985. In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Human monoclonal antibodies may be utilized in the practice of the invention and may be produced by using human hybridomas (*see, e.g.,* Cote, *et al.,* 1983. *Proc Natl Acad Sci USA* 80: 2026-2030) or by transforming human B-cells with Epstein Barr Virus *in vitro* (*see, e.g.,* Cole, *et al.,* 1985. In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Each of the above citations is incorporated herein by reference in their entirety.

According to the invention, techniques can be adapted for the production of single-chain antibodies specific to an FCTRX protein (*see, e.g.,* U.S. Patent No. 4,946,778). In addition, methods can be adapted for the construction of F_{ab} expression libraries (*see, e.g.,* Huse, *et al.,* 1989. *Science* 246: 1275-1281) to allow rapid and effective identification of monoclonal F_{ab} fragments with the desired specificity for an FCTRX protein or derivatives, fragments, analogs or homologs thereof. Non-human antibodies can be "humanized" by techniques well known in the art. *See, e.g.,* U.S. Patent No. 5,225,539. Antibody fragments that contain the idiotypes to an FCTRX protein may be produced by techniques known in the art including, but not limited to: (*i*) an $F_{(ab')2}$ fragment produced by pepsin digestion of an antibody molecule; (*ii*) an F_{ab} fragment generated by reducing the disulfide bridges of an $F_{(ab')2}$ fragment; (*iii*) an F_{ab} fragment generated by the treatment of the antibody molecule with papain and a reducing agent; and (*iv*) F_v fragments.

Additionally, recombinant anti-FCTRX antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made

using standard recombinant DNA techniques, are within the scope of the invention. Such chimeric and humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art, for example using methods described in International Application No. PCT/US86/02269; European Patent Application No. 184,187; European Patent Application No. 171,496; European Patent Application No. 173,494; PCT International Publication No. WO 86/01533; U.S. Patent No. 4,816,567; U.S. Pat. No. 5,225,539; European Patent Application No. 125,023; Better, *et al.*, 1988. *Science* 240: 1041-1043; Liu, *et al.*, 1987. *Proc. Natl. Acad. Sci. USA* 84: 3439-3443; Liu, *et al.*, 1987. *J. Immunol.* 139: 3521-3526; Sun, *et al.*, 1987. *Proc. Natl. Acad. Sci. USA* 84: 214-218; Nishimura, *et al.*, 1987. *Cancer Res.* 47: 999-1005; Wood, *et al.*, 1985. *Nature* 314 :446-449; Shaw, *et al.*, 1988. *J. Natl. Cancer Inst.* 80: 1553-1559); Morrison(1985) *Science* 229:1202-1207; Oi, *et al.* (1986) *BioTechniques* 4:214; Jones, *et al.*, 1986. *Nature* 321: 552-525; Verhoeyan, *et al.*, 1988. *Science* 239: 1534; and Beidler, *et al.*, 1988. *J. Immunol.* 141: 4053-4060. Each of the above citations are incorporated herein by reference in their entirety.

In one embodiment, methods for the screening of antibodies that possess the desired specificity include, but are not limited to, enzyme-linked immunosorbent assay (ELISA) and other immunologically-mediated techniques known within the art. In a specific embodiment, selection of antibodies that are specific to a particular domain of an FCTRX protein is facilitated by generation of hybridomas that bind to the fragment of an FCTRX protein possessing such a domain. Thus, antibodies that are specific for a desired domain within an FCTRX protein, or derivatives, fragments, analogs or homologs thereof, are also provided herein.

Anti-FCTRX antibodies may be used in methods known within the art relating to the localization and/or quantitation of an FCTRX protein (*e.g.,* for use in measuring levels of the FCTRX protein within appropriate physiological samples, for use in diagnostic methods, for use in imaging the protein, and the like). In a given embodiment, antibodies for FCTRX proteins, or derivatives, fragments, analogs or homologs thereof, that contain the antibody derived binding domain, are utilized as pharmacologically-active compounds (hereinafter "Therapeutics").

An anti-FCTRX antibody (*e.g.*, monoclonal antibody) can be used to isolate an FCTRX polypeptide by standard techniques, such as affinity chromatography or immunoprecipitation. An anti-FCTRX antibody can facilitate the purification of natural FCTRX polypeptide from cells and of recombinantly-produced FCTRX polypeptide expressed in host cells. Moreover, an anti-FCTRX antibody can be used to detect FCTRX protein (*e.g.*, in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the FCTRX protein. Anti-FCTRX antibodies can be used diagnostically to monitor protein levels in tissue as part of a

clinical testing procedure, *e.g.*, to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling (*i.e.*, physically linking) the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, β-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include ^{125}I, ^{131}I, ^{35}S or ^{3}H.

FCTRX Recombinant Expression Vectors and Host Cells

Another aspect of the invention pertains to vectors, preferably expression vectors, containing a nucleic acid encoding an FCTRX protein, or derivatives, fragments, analogs or homologs thereof. As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (*e.g.*, bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (*e.g.*, non-episomal mammalian vectors) are integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they are operatively-linked. Such vectors are referred to herein as "expression vectors". In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. In the present specification, "plasmid" and "vector" can be used interchangeably as the plasmid is the most commonly used form of vector. However, the invention is intended to include such other forms of expression vectors, such as viral vectors (*e.g.*, replication defective retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell, which means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis

of the host cells to be used for expression, that is operatively-linked to the nucleic acid sequence to be expressed. Within a recombinant expression vector, "operably-linked" is intended to mean that the nucleotide sequence of interest is linked to the regulatory sequence(s) in a manner that allows for expression of the nucleotide sequence (*e.g.*, in an *in vitro* transcription/translation system or in a host cell when the vector is introduced into the host cell).

The term "regulatory sequence" is intended to includes promoters, enhancers and other expression control elements (*e.g.*, polyadenylation signals). Such regulatory sequences are described, for example, in Goeddel, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990). Regulatory sequences include those that direct constitutive expression of a nucleotide sequence in many types of host cell and those that direct expression of the nucleotide sequence only in certain host cells (*e.g.*, tissue-specific regulatory sequences). It will be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired, etc. The expression vectors of the invention can be introduced into host cells to thereby produce proteins or peptides, including fusion proteins or peptides, encoded by nucleic acids as described herein (*e.g.*, FCTRX proteins, mutant forms of FCTRX proteins, fusion proteins, etc.).

The recombinant expression vectors of the invention can be designed for expression of FCTRX proteins in prokaryotic or eukaryotic cells. For example, FCTRX proteins can be expressed in bacterial cells such as *Escherichia coli*, insect cells (using baculovirus expression vectors) yeast cells or mammalian cells. Suitable host cells are discussed further in Goeddel, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990). Alternatively, the recombinant expression vector can be transcribed and translated *in vitro*, for example using T7 promoter regulatory sequences and T7 polymerase.

Expression of proteins in prokaryotes is most often carried out in *Escherichia coli* with vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion proteins. Fusion vectors add a number of amino acids to a protein encoded therein, usually to the amino terminus of the recombinant protein. Such fusion vectors typically serve three purposes: (*i*) to increase expression of recombinant protein; (*ii*) to increase the solubility of the recombinant protein; and (*iii*) to aid in the purification of the recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa,

thrombin and enterokinase. Typical fusion expression vectors include pGEX (Pharmacia Biotech Inc; Smith and Johnson, 1988. *Gene* 67: 31-40), pMAL (New England Biolabs, Beverly, Mass.) and pRIT5 (Pharmacia, Piscataway, N.J.) that fuse glutathione S-transferase (GST), maltose E binding protein, or protein A, respectively, to the target recombinant protein.

Examples of suitable inducible non-fusion *E. coli* expression vectors include pTrc (Amrann *et al.*, (1988) *Gene* 69:301-315) and pET 11d (Studier *et al.*, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990) 60-89).

One strategy to maximize recombinant protein expression in *E. coli* is to express the protein in a host bacteria with an impaired capacity to proteolytically cleave the recombinant protein. *See, e.g.,* Gottesman, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990) 119-128. Another strategy is to alter the nucleic acid sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in *E. coli* (*see, e.g.,* Wada, *et al.*, 1992. *Nucl. Acids Res.* 20: 2111-2118). Such alteration of nucleic acid sequences of the invention can be carried out by standard DNA synthesis techniques.

In another embodiment, the FCTRX expression vector is a yeast expression vector. Examples of vectors for expression in yeast *Saccharomyces cerivisae* include pYepSec1 (Baldari, *et al.*, 1987. *EMBO J.* 6: 229-234), pMFa (Kurjan and Herskowitz, 1982. *Cell* 30: 933-943), pJRY88 (Schultz *et al.*, 1987. *Gene* 54: 113-123), pYES2 (Invitrogen Corporation, San Diego, Calif.), and picZ (InVitrogen Corp, San Diego, Calif.).

Alternatively, FCTRX can be expressed in insect cells using baculovirus expression vectors. Baculovirus vectors available for expression of proteins in cultured insect cells (*e.g.*, SF9 cells) include the pAc series (Smith, *et al.*, 1983. *Mol. Cell. Biol.* 3: 2156-2165) and the pVL series (Lucklow and Summers, 1989. *Virology* 170: 31-39).

In yet another embodiment, a nucleic acid of the invention is expressed in mammalian cells using a mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed, 1987. *Nature* 329: 840) and pMT2PC (Kaufman, *et al.*, 1987. *EMBO J.* 6: 187-195). When used in mammalian cells, the expression vector's control functions are often provided by viral regulatory elements. For example, commonly used promoters are derived from polyoma, adenovirus 2, cytomegalovirus, and simian virus 40. For other suitable expression systems for both prokaryotic and eukaryotic cells see, *e.g.*, Chapters 16 and 17 of Sambrook, *et al.*, MOLECULAR CLONING: A LABORATORY MANUAL. 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1989.

In another embodiment, the recombinant mammalian expression vector is capable of directing expression of the nucleic acid preferentially in a particular cell type (*e.g.*, tissue-specific regulatory elements are used to express the nucleic acid). Tissue-specific regulatory elements are known in the art. Non-limiting examples of suitable tissue-specific promoters include the albumin promoter (liver-specific; Pinkert, *et al.*, 1987. *Genes Dev.* 1: 268-277), lymphoid-specific promoters (Calame and Eaton, 1988. *Adv. Immunol.* 43: 235-275), in particular promoters of T cell receptors (Winoto and Baltimore, 1989. *EMBO J.* 8: 729-733) and immunoglobulins (Banerji, *et al.*, 1983. *Cell* 33: 729-740; Queen and Baltimore, 1983. *Cell* 33: 741-748), neuron-specific promoters (*e.g.*, the neurofilament promoter; Byrne and Ruddle, 1989. *Proc. Natl. Acad. Sci. USA* 86: 5473-5477), pancreas-specific promoters (Edlund, *et al.*, 1985. *Science* 230: 912-916), and mammary gland-specific promoters (*e.g.*, milk whey promoter; U.S. Pat. No. 4,873,316 and European Application Publication No. 264,166). Developmentally-regulated promoters are also encompassed, *e.g.*, the murine hox promoters (Kessel and Gruss, 1990. *Science* 249: 374-379) and the α-fetoprotein promoter (Campes and Tilghman, 1989. *Genes Dev.* 3: 537-546).

The invention further provides a recombinant expression vector comprising a DNA molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operatively-linked to a regulatory sequence in a manner that allows for expression (by transcription of the DNA molecule) of an RNA molecule that is antisense to FCTRX mRNA. Regulatory sequences operatively linked to a nucleic acid cloned in the antisense orientation can be chosen that direct the continuous expression of the antisense RNA molecule in a variety of cell types, for instance viral promoters and/or enhancers, or regulatory sequences can be chosen that direct constitutive, tissue specific or cell type specific expression of antisense RNA. The antisense expression vector can be in the form of a recombinant plasmid, phagemid or attenuated virus in which antisense nucleic acids are produced under the control of a high efficiency regulatory region, the activity of which can be determined by the cell type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense genes *see, e.g.,* Weintraub, *et al.*, "Antisense RNA as a molecular tool for genetic analysis," *Reviews-Trends in Genetics*, Vol. 1(1) 1986.

Another aspect of the invention pertains to host cells into which a recombinant expression vector of the invention has been introduced. The terms "host cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but also to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental

influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

A host cell can be any prokaryotic or eukaryotic cell. For example, FCTRX protein can be expressed in bacterial cells such as *E. coli*, insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells). Other suitable host cells are known to those skilled in the art.

Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional transformation or transfection techniques. As used herein, the terms "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid (*e.g.*, DNA) into a host cell, including calcium phosphate or calcium chloride co-precipitation, DEAE-dextran-mediated transfection, lipofection, or electroporation. Suitable methods for transforming or transfecting host cells can be found in Sambrook, *et al.* (MOLECULAR CLONING: A LABORATORY MANUAL. 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1989), and other laboratory manuals.

For stable transfection of mammalian cells, it is known that, depending upon the expression vector and transfection technique used, only a small fraction of cells may integrate the foreign DNA into their genome. In order to identify and select these integrants, a gene that encodes a selectable marker (*e.g.*, resistance to antibiotics) is generally introduced into the host cells along with the gene of interest. Various selectable markers include those that confer resistance to drugs, such as G418, hygromycin and methotrexate. Nucleic acid encoding a selectable marker can be introduced into a host cell on the same vector as that encoding FCTRX or can be introduced on a separate vector. Cells stably transfected with the introduced nucleic acid can be identified by drug selection (*e.g.*, cells that have incorporated the selectable marker gene will survive, while the other cells die).

A host cell of the invention, such as a prokaryotic or eukaryotic host cell in culture, can be used to produce (*i.e.*, express) FCTRX protein. Accordingly, the invention further provides methods for producing FCTRX protein using the host cells of the invention. In one embodiment, the method comprises culturing the host cell of invention (into which a recombinant expression vector encoding FCTRX protein has been introduced) in a suitable medium such that FCTRX protein is produced. In another embodiment, the method further comprises isolating FCTRX protein from the medium or the host cell.

Transgenic FCTRX Animals

The host cells of the invention can also be used to produce non-human transgenic animals. For example, in one embodiment, a host cell of the invention is a fertilized oocyte or an embryonic stem cell into which FCTRX protein-coding sequences have been introduced. Such host cells can then be used to create non-human transgenic animals in which exogenous FCTRX sequences have been introduced into their genome or homologous recombinant animals in which endogenous FCTRX sequences have been altered. Such animals are useful for studying the function and/or activity of FCTRX protein and for identifying and/or evaluating modulators of FCTRX protein activity. As used herein, a "transgenic animal" is a non-human animal, preferably a mammal, more preferably a rodent such as a rat or mouse, in which one or more of the cells of the animal includes a transgene. Other examples of transgenic animals include non-human primates, sheep, dogs, cows, goats, chickens, amphibians, etc. A transgene is exogenous DNA that is integrated into the genome of a cell from which a transgenic animal develops and that remains in the genome of the mature animal, thereby directing the expression of an encoded gene product in one or more cell types or tissues of the transgenic animal. As used herein, a "homologous recombinant animal" is a non-human animal, preferably a mammal, more preferably a mouse, in which an endogenous FCTRX gene has been altered by homologous recombination between the endogenous gene and an exogenous DNA molecule introduced into a cell of the animal, *e.g.*, an embryonic cell of the animal, prior to development of the animal.

A transgenic animal of the invention can be created by introducing FCTRX-encoding nucleic acid into the male pronuclei of a fertilized oocyte (*e.g.*, by microinjection, retroviral infection) and allowing the oocyte to develop in a pseudopregnant female foster animal. The human FCTRX cDNA sequences of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, can be introduced as a transgene into the genome of a non-human animal. Alternatively, a non-human homologue of the human FCTRX gene, such as a mouse FCTRX gene, can be isolated based on hybridization to the human FCTRX cDNA (described further *supra*) and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably-linked to the FCTRX transgene to direct expression of FCTRX protein to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866; 4,870,009; and 4,873,191; and Hogan, 1986. In: MANIPULATING THE MOUSE EMBRYO, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. Similar methods are used for production of other transgenic animals. A

transgenic founder animal can be identified based upon the presence of the FCTRX transgene in its genome and/or expression of FCTRX mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene-encoding FCTRX protein can further be bred to other transgenic animals carrying other transgenes.

To create a homologous recombinant animal, a vector is prepared which contains at least a portion of an FCTRX gene into which a deletion, addition or substitution has been introduced to thereby alter, *e.g.*, functionally disrupt, the FCTRX gene. The FCTRX gene can be a human gene (*e.g.*, the cDNA of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24), but more preferably, is a non-human homologue of a human FCTRX gene. For example, a mouse homologue of human FCTRX gene of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, can be used to construct a homologous recombination vector suitable for altering an endogenous FCTRX gene in the mouse genome. In one embodiment, the vector is designed such that, upon homologous recombination, the endogenous FCTRX gene is functionally disrupted (*i.e.*, no longer encodes a functional protein; also referred to as a "knock out" vector).

Alternatively, the vector can be designed such that, upon homologous recombination, the endogenous FCTRX gene is mutated or otherwise altered but still encodes functional protein (*e.g.*, the upstream regulatory region can be altered to thereby alter the expression of the endogenous FCTRX protein). In the homologous recombination vector, the altered portion of the FCTRX gene is flanked at its 5'- and 3'-termini by additional nucleic acid of the FCTRX gene to allow for homologous recombination to occur between the exogenous FCTRX gene carried by the vector and an endogenous FCTRX gene in an embryonic stem cell. The additional flanking FCTRX nucleic acid is of sufficient length for successful homologous recombination with the endogenous gene. Typically, several kilobases of flanking DNA (both at the 5'- and 3'-termini) are included in the vector. *See, e.g.,* Thomas, *et al.*, 1987. *Cell* 51: 503 for a description of homologous recombination vectors. The vector is ten introduced into an embryonic stem cell line (*e.g.*, by electroporation) and cells in which the introduced FCTRX gene has homologously-recombined with the endogenous FCTRX gene are selected. *See, e.g.*, Li, *et al.*, 1992. *Cell* 69: 915.

The selected cells are then injected into a blastocyst of an animal (*e.g.*, a mouse) to form aggregation chimeras. *See, e.g.*, Bradley, 1987. In: TERATOCARCINOMAS AND EMBRYONIC STEM CELLS: A PRACTICAL APPROACH, Robertson, ed. IRL, Oxford, pp. 113-152. A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and the embryo brought to term. Progeny harboring the homologously-recombined DNA in their germ cells can

be used to breed animals in which all cells of the animal contain homologously-recombined DNA by germline transmission of the transgene. Methods for constructing homologous recombination vectors and homologous recombinant animals are described further in Bradley, 1991. *Curr. Opin. Biotechnol.* 2: 823-829; PCT International Publication Nos.: WO 90/11354; WO 91/01140; WO 92/0968; and WO 93/04169.

In another embodiment, transgenic non-humans animals can be produced that contain selected systems that allow for regulated expression of the transgene. One example of such a system is the cre/loxP recombinase system of bacteriophage P1. For a description of the cre/loxP recombinase system, *See, e.g.*, Lakso, *et al.*, 1992. *Proc. Natl. Acad. Sci. USA* 89: 6232-6236. Another example of a recombinase system is the FLP recombinase system of *Saccharomyces cerevisiae. See,* O'Gorman, *et al.*, 1991. *Science* 251:1351-1355. If a cre/loxP recombinase system is used to regulate expression of the transgene, animals containing transgenes encoding both the Cre recombinase and a selected protein are required. Such animals can be provided through the construction of "double" transgenic animals, *e.g.*, by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase.

Clones of the non-human transgenic animals described herein can also be produced according to the methods described in Wilmut, *et al.*, 1997. *Nature* 385: 810-813. In brief, a cell (*e.g.*, a somatic cell) from the transgenic animal can be isolated and induced to exit the growth cycle and enter G_0 phase. The quiescent cell can then be fused, *e.g.*, through the use of electrical pulses, to an enucleated oocyte from an animal of the same species from which the quiescent cell is isolated. The reconstructed oocyte is then cultured such that it develops to morula or blastocyte and then transferred to pseudopregnant female foster animal. The offspring borne of this female foster animal will be a clone of the animal from which the cell (*e.g.*, the somatic cell) is isolated.

Pharmaceutical Compositions

The FCTRX nucleic acid molecules, FCTRX proteins, and anti-FCTRX antibodies (also referred to herein as "active compounds") of the invention, and derivatives, fragments, analogs and homologs thereof, can be incorporated into pharmaceutical compositions suitable for administration. Such compositions typically comprise the nucleic acid molecule, protein, or antibody and a pharmaceutically acceptable carrier. As used herein, "pharmaceutically acceptable carrier" is intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like,

compatible with pharmaceutical administration. Suitable carriers are described in the most recent edition of Remington's Pharmaceutical Sciences, a standard reference text in the field, which is incorporated herein by reference. Preferred examples of such carriers or diluents include, but are not limited to, water, saline, finger's solutions, dextrose solution, and 5% human serum albumin. Liposomes and non-aqueous vehicles such as fixed oils may also be used. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds can also be incorporated into the compositions.

A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, *e.g.*, intravenous, intradermal, subcutaneous, oral (*e.g.*, inhalation), transdermal (*i.e.,* topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid (EDTA); buffers such as acetates, citrates or phosphates, and agents for the adjustment of tonicity such as sodium chloride or dextrose. The pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF, Parsippany, N.J.) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy syringeability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the

action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as manitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions can be prepared by incorporating the active compound (*e.g.*, an FCTRX protein or anti-FCTRX antibody) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle that contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, methods of preparation are vacuum drying and freeze-drying that yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

For administration by inhalation, the compounds are delivered in the form of an aerosol spray from pressured container or dispenser which contains a suitable propellant, *e.g.*, a gas such as carbon dioxide, or a nebulizer.

Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for

example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art.

The compounds can also be prepared in the form of suppositories (*e.g.*, with conventional suppository bases such as cocoa butter and other glycerides) or retention enemas for rectal delivery.

In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. The materials can also be obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) can also be used as pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

It is especially advantageous to formulate oral or parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the active compound and the particular therapeutic effect to be achieved, and the limitations inherent in the art of compounding such an active compound for the treatment of individuals.

The nucleic acid molecules of the invention can be inserted into vectors and used as gene therapy vectors. Gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (*see, e.g.,* U.S. Patent No. 5,328,470) or by stereotactic injection (*see, e.g.*, Chen, *et al.*, 1994. *Proc. Natl. Acad. Sci. USA* 91: 3054-3057). The pharmaceutical preparation of the gene therapy vector can include the gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. Alternatively, where the complete gene delivery vector can be produced intact from recombinant

cells, *e.g.*, retroviral vectors, the pharmaceutical preparation can include one or more cells that produce the gene delivery system.

The pharmaceutical compositions can be included in a container, pack, or dispenser together with instructions for administration.

Screening and Detection Methods

The isolated nucleic acid molecules of the invention can be used to express FCTRX protein (*e.g.*, via a recombinant expression vector in a host cell in gene therapy applications), to detect FCTRX mRNA (*e.g.*, in a biological sample) or a genetic lesion in an FCTRX gene, and to modulate FCTRX activity, as described further, below. In addition, the FCTRX proteins can be used to screen drugs or compounds that modulate the FCTRX protein activity or expression as well as to treat disorders characterized by insufficient or excessive production of FCTRX protein or production of FCTRX protein forms that have decreased or aberrant activity compared to FCTRX wild-type protein (*e.g.*; diabetes (regulates insulin release); obesity (binds and transport lipids); metabolic disturbances associated with obesity, the metabolic syndrome X as well as anorexia and wasting disorders associated with chronic diseases and various cancers, and infectious disease(possesses anti-microbial activity) and the various dyslipidemias. In addition, the anti-FCTRX antibodies of the invention can be used to detect and isolate FCTRX proteins and modulate FCTRX activity. In yet a further aspect, the invention can be used in methods to influence appetite, absorption of nutrients and the disposition of metabolic substrates in both a positive and negative fashion.

The invention further pertains to novel agents identified by the screening assays described herein and uses thereof for treatments as described, *supra*.

Screening Assays

The invention provides a method (also referred to herein as a "screening assay") for identifying modulators, *i.e.*, candidate or test compounds or agents (*e.g.*, peptides, peptidomimetics, small molecules or other drugs) that bind to FCTRX proteins or have a stimulatory or inhibitory effect on, *e.g.*, FCTRX protein expression or FCTRX protein activity. The invention also includes compounds identified in the screening assays described herein.

In one embodiment, the invention provides assays for screening candidate or test compounds which bind to or modulate the activity of the membrane-bound form of an FCTRX protein or polypeptide or biologically-active portion thereof. The test compounds of the invention can be obtained using any of the numerous approaches in combinatorial library methods known in the art, including: biological libraries; spatially addressable parallel solid

phase or solution phase libraries; synthetic library methods requiring deconvolution; the "one-bead one-compound" library method; and synthetic library methods using affinity chromatography selection. The biological library approach is limited to peptide libraries, while the other four approaches are applicable to peptide, non-peptide oligomer or small molecule libraries of compounds. *See, e.g.,* Lam, 1997. *Anticancer Drug Design* 12: 145.

A "small molecule" as used herein, is meant to refer to a composition that has a molecular weight of less than about 5 kD and most preferably less than about 4 kD. Small molecules can be, *e.g.*, nucleic acids, peptides, polypeptides, peptidomimetics, carbohydrates, lipids or other organic or inorganic molecules. Libraries of chemical and/or biological mixtures, such as fungal, bacterial, or algal extracts, are known in the art and can be screened with any of the assays of the invention.

Examples of methods for the synthesis of molecular libraries can be found in the art, for example in: DeWitt, *et al.*, 1993. *Proc. Natl. Acad. Sci. U.S.A.* 90: 6909; Erb, *et al.*, 1994. *Proc. Natl. Acad. Sci. U.S.A.* 91: 11422; Zuckermann, *et al.*, 1994. *J. Med. Chem.* 37: 2678; Cho, *et al.*, 1993. *Science* 261: 1303; Carrell, *et al.*, 1994. *Angew. Chem. Int. Ed. Engl.* 33: 2059; Carell, *et al.*, 1994. *Angew. Chem. Int. Ed. Engl.* 33: 2061; and Gallop, *et al.*, 1994. *J. Med. Chem.* 37: 1233.

Libraries of compounds may be presented in solution (*e.g.*, Houghten, 1992. *Biotechniques* 13: 412-421), or on beads (Lam, 1991. *Nature* 354: 82-84), on chips (Fodor, 1993. *Nature* 364: 555-556), bacteria (Ladner, U.S. Patent No. 5,223,409), spores (Ladner, U.S. Patent 5,233,409), plasmids (Cull, *et al.*, 1992. *Proc. Natl. Acad. Sci. USA* 89: 1865-1869) or on phage (Scott and Smith, 1990. *Science* 249: 386-390; Devlin, 1990. *Science* 249: 404-406; Cwirla, *et al.*, 1990. *Proc. Natl. Acad. Sci. U.S.A.* 87: 6378-6382; Felici, 1991. *J. Mol. Biol.* 222: 301-310; Ladner, U.S. Patent No. 5,233,409.).

In one embodiment, an assay is a cell-based assay in which a cell which expresses a membrane-bound form of FCTRX protein, or a biologically-active portion thereof, on the cell surface is contacted with a test compound and the ability of the test compound to bind to an FCTRX protein determined. The cell, for example, can of mammalian origin or a yeast cell. Determining the ability of the test compound to bind to the FCTRX protein can be accomplished, for example, by coupling the test compound with a radioisotope or enzymatic label such that binding of the test compound to the FCTRX protein or biologically-active portion thereof can be determined by detecting the labeled compound in a complex. For example, test compounds can be labeled with ^{125}I, ^{35}S, ^{14}C, or ^{3}H, either directly or indirectly, and the radioisotope detected by direct counting of radioemission or by scintillation counting. Alternatively, test compounds can

be enzymatically-labeled with, for example, horseradish peroxidase, alkaline phosphatase, or luciferase, and the enzymatic label detected by determination of conversion of an appropriate substrate to product. In one embodiment, the assay comprises contacting a cell which expresses a membrane-bound form of FCTRX protein, or a biologically-active portion thereof, on the cell surface with a known compound which binds FCTRX to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with an FCTRX protein, wherein determining the ability of the test compound to interact with an FCTRX protein comprises determining the ability of the test compound to preferentially bind to FCTRX protein or a biologically-active portion thereof as compared to the known compound.

In another embodiment, an assay is a cell-based assay comprising contacting a cell expressing a membrane-bound form of FCTRX protein, or a biologically-active portion thereof, on the cell surface with a test compound and determining the ability of the test compound to modulate (*e.g.*, stimulate or inhibit) the activity of the FCTRX protein or biologically-active portion thereof. Determining the ability of the test compound to modulate the activity of FCTRX or a biologically-active portion thereof can be accomplished, for example, by determining the ability of the FCTRX protein to bind to or interact with an FCTRX target molecule. As used herein, a "target molecule" is a molecule with which an FCTRX protein binds or interacts in nature, for example, a molecule on the surface of a cell which expresses an FCTRX interacting protein, a molecule on the surface of a second cell, a molecule in the extracellular milieu, a molecule associated with the internal surface of a cell membrane or a cytoplasmic molecule. An FCTRX target molecule can be a non-FCTRX molecule or an FCTRX protein or polypeptide of the invention. In one embodiment, an FCTRX target molecule is a component of a signal transduction pathway that facilitates transduction of an extracellular signal (*e.g.* a signal generated by binding of a compound to a membrane-bound FCTRX molecule) through the cell membrane and into the cell. The target, for example, can be a second intercellular protein that has catalytic activity or a protein that facilitates the association of downstream signaling molecules with FCTRX.

Determining the ability of the FCTRX protein to bind to or interact with an FCTRX target molecule can be accomplished by one of the methods described above for determining direct binding. In one embodiment, determining the ability of the FCTRX protein to bind to or interact with an FCTRX target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by detecting induction of a cellular second messenger of the target (*i.e.* intracellular Ca^{2+}, diacylglycerol, IP_3, etc.), detecting catalytic/enzymatic activity of the target an appropriate substrate, detecting the

induction of a reporter gene (comprising an FCTRX-responsive regulatory element operatively linked to a nucleic acid encoding a detectable marker, *e.g.*, luciferase), or detecting a cellular response, for example, cell survival, cellular differentiation, or cell proliferation.

In yet another embodiment, an assay of the invention is a cell-free assay comprising contacting an FCTRX protein or biologically-active portion thereof with a test compound and determining the ability of the test compound to bind to the FCTRX protein or biologically-active portion thereof. Binding of the test compound to the FCTRX protein can be determined either directly or indirectly as described above. In one such embodiment, the assay comprises contacting the FCTRX protein or biologically-active portion thereof with a known compound which binds FCTRX to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with an FCTRX protein, wherein determining the ability of the test compound to interact with an FCTRX protein comprises determining the ability of the test compound to preferentially bind to FCTRX or biologically-active portion thereof as compared to the known compound.

In still another embodiment, an assay is a cell-free assay comprising contacting FCTRX protein or biologically-active portion thereof with a test compound and determining the ability of the test compound to modulate (*e.g.* stimulate or inhibit) the activity of the FCTRX protein or biologically-active portion thereof. Determining the ability of the test compound to modulate the activity of FCTRX can be accomplished, for example, by determining the ability of the FCTRX protein to bind to an FCTRX target molecule by one of the methods described above for determining direct binding. In an alternative embodiment, determining the ability of the test compound to modulate the activity of FCTRX protein can be accomplished by determining the ability of the FCTRX protein further modulate an FCTRX target molecule. For example, the catalytic/enzymatic activity of the target molecule on an appropriate substrate can be determined as described, *supra*.

In yet another embodiment, the cell-free assay comprises contacting the FCTRX protein or biologically-active portion thereof with a known compound which binds FCTRX protein to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with an FCTRX protein, wherein determining the ability of the test compound to interact with an FCTRX protein comprises determining the ability of the FCTRX protein to preferentially bind to or modulate the activity of an FCTRX target molecule.

The cell-free assays of the invention are amenable to use of both the soluble form or the membrane-bound form of FCTRX protein. In the case of cell-free assays comprising the membrane-bound form of FCTRX protein, it may be desirable to utilize a solubilizing agent such

that the membrane-bound form of FCTRX protein is maintained in solution. Examples of such solubilizing agents include non-ionic detergents such as n-octylglucoside, n-dodecylglucoside, n-dodecylmaltoside, octanoyl-N-methylglucamide, decanoyl-N-methylglucamide, Triton® X-100, Triton® X-114, Thesit®, Isotridecypoly(ethylene glycol ether)$_n$, N-dodecyl--N,N-dimethyl-3-ammonio-1-propane sulfonate, 3-(3-cholamidopropyl) dimethylamminiol-1-propane sulfonate (CHAPS), or 3-(3-cholamidopropyl)dimethylamminiol-2-hydroxy-1-propane sulfonate (CHAPSO).

In more than one embodiment of the above assay methods of the invention, it may be desirable to immobilize either FCTRX protein or its target molecule to facilitate separation of complexed from uncomplexed forms of one or both of the proteins, as well as to accommodate automation of the assay. Binding of a test compound to FCTRX protein, or interaction of FCTRX protein with a target molecule in the presence and absence of a candidate compound, can be accomplished in any vessel suitable for containing the reactants. Examples of such vessels include microtiter plates, test tubes, and micro-centrifuge tubes. In one embodiment, a fusion protein can be provided that adds a domain that allows one or both of the proteins to be bound to a matrix. For example, GST-FCTRX fusion proteins or GST-target fusion proteins can be adsorbed onto glutathione sepharose beads (Sigma Chemical, St. Louis, MO) or glutathione derivatized microtiter plates, that are then combined with the test compound or the test compound and either the non-adsorbed target protein or FCTRX protein, and the mixture is incubated under conditions conducive to complex formation (*e.g.*, at physiological conditions for salt and pH). Following incubation, the beads or microtiter plate wells are washed to remove any unbound components, the matrix immobilized in the case of beads, complex determined either directly or indirectly, for example, as described, *supra*. Alternatively, the complexes can be dissociated from the matrix, and the level of FCTRX protein binding or activity determined using standard techniques.

Other techniques for immobilizing proteins on matrices can also be used in the screening assays of the invention. For example, either the FCTRX protein or its target molecule can be immobilized utilizing conjugation of biotin and streptavidin. Biotinylated FCTRX protein or target molecules can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques well-known within the art (*e.g.*, biotinylation kit, Pierce Chemicals, Rockford, Ill.), and immobilized in the wells of streptavidin-coated 96 well plates (Pierce Chemical). Alternatively, antibodies reactive with FCTRX protein or target molecules, but which do not interfere with binding of the FCTRX protein to its target molecule, can be derivatized to the wells of the plate, and unbound target or FCTRX protein trapped in the wells by antibody conjugation. Methods

for detecting such complexes, in addition to those described above for the GST-immobilized complexes, include immunodetection of complexes using antibodies reactive with the FCTRX protein or target molecule, as well as enzyme-linked assays that rely on detecting an enzymatic activity associated with the FCTRX protein or target molecule.

In another embodiment, modulators of FCTRX protein expression are identified in a method wherein a cell is contacted with a candidate compound and the expression of FCTRX mRNA or protein in the cell is determined. The level of expression of FCTRX mRNA or protein in the presence of the candidate compound is compared to the level of expression of FCTRX mRNA or protein in the absence of the candidate compound. The candidate compound can then be identified as a modulator of FCTRX mRNA or protein expression based upon this comparison. For example, when expression of FCTRX mRNA or protein is greater (*i.e.*, statistically significantly greater) in the presence of the candidate compound than in its absence, the candidate compound is identified as a stimulator of FCTRX mRNA or protein expression. Alternatively, when expression of FCTRX mRNA or protein is less (statistically significantly less) in the presence of the candidate compound than in its absence, the candidate compound is identified as an inhibitor of FCTRX mRNA or protein expression. The level of FCTRX mRNA or protein expression in the cells can be determined by methods described herein for detecting FCTRX mRNA or protein.

In yet another aspect of the invention, the FCTRX proteins can be used as "bait proteins" in a two-hybrid assay or three hybrid assay (*see, e.g.*, U.S. Patent No. 5,283,317; Zervos, *et al.*, 1993. *Cell* 72: 223-232; Madura, *et al.*, 1993. *J. Biol. Chem.* 268: 12046-12054; Bartel, *et al.*, 1993. *Biotechniques* 14: 920-924; Iwabuchi, *et al.*, 1993. *Oncogene* 8: 1693-1696; and Brent WO 94/10300), to identify other proteins that bind to or interact with FCTRX ("FCTRX-binding proteins" or "FCTRX-bp") and modulate FCTRX activity. Such FCTRX-binding proteins are also likely to be involved in the propagation of signals by the FCTRX proteins as, for example, upstream or downstream elements of the FCTRX pathway.

The two-hybrid system is based on the modular nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. In one construct, the gene that codes for FCTRX is fused to a gene encoding the DNA binding domain of a known transcription factor (*e.g.*, GAL-4). In the other construct, a DNA sequence, from a library of DNA sequences, that encodes an unidentified protein ("prey" or "sample") is fused to a gene that codes for the activation domain of the known transcription factor. If the "bait" and the "prey" proteins are able to interact, *in vivo*, forming an FCTRX-dependent complex, the DNA-binding and activation domains of the transcription factor

are brought into close proximity. This proximity allows transcription of a reporter gene (*e.g.*, LacZ) that is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be detected and cell colonies containing the functional transcription factor can be isolated and used to obtain the cloned gene that encodes the protein which interacts with FCTRX.

The invention further pertains to novel agents identified by the aforementioned screening assays and uses thereof for treatments as described herein.

Detection Assays

Portions or fragments of the cDNA sequences identified herein (and the corresponding complete gene sequences) can be used in numerous ways as polynucleotide reagents. By way of example, and not of limitation, these sequences can be used to: (*i*) map their respective genes on a chromosome; and, thus, locate gene regions associated with genetic disease; (*ii*) identify an individual from a minute biological sample (tissue typing); and (*iii*) aid in forensic identification of a biological sample. Some of these applications are described in the subsections, below.

Chromosome Mapping

Once the sequence (or a portion of the sequence) of a gene has been isolated, this sequence can be used to map the location of the gene on a chromosome. This process is called chromosome mapping. Accordingly, portions or fragments of the FCTRX sequences, SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments or derivatives thereof, can be used to map the location of the FCTRX genes, respectively, on a chromosome. The mapping of the FCTRX sequences to chromosomes is an important first step in correlating these sequences with genes associated with disease.

Briefly, FCTRX genes can be mapped to chromosomes by preparing PCR primers (preferably 15-25 bp in length) from the FCTRX sequences. Computer analysis of the FCTRX, sequences can be used to rapidly select primers that do not span more than one exon in the genomic DNA, thus complicating the amplification process. These primers can then be used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the FCTRX sequences will yield an amplified fragment.

Somatic cell hybrids are prepared by fusing somatic cells from different mammals (*e.g.*, human and mouse cells). As hybrids of human and mouse cells grow and divide, they gradually lose human chromosomes in random order, but retain the mouse chromosomes. By using media in which mouse cells cannot grow, because they lack a particular enzyme, but in which human

cells can, the one human chromosome that contains the gene encoding the needed enzyme will be retained. By using various media, panels of hybrid cell lines can be established. Each cell line in a panel contains either a single human chromosome or a small number of human chromosomes, and a full set of mouse chromosomes, allowing easy mapping of individual genes to specific human chromosomes. *See, e.g.,* D'Eustachio, *et al.*, 1983. *Science* 220: 919-924. Somatic cell hybrids containing only fragments of human chromosomes can also be produced by using human chromosomes with translocations and deletions.

PCR mapping of somatic cell hybrids is a rapid procedure for assigning a particular sequence to a particular chromosome. Three or more sequences can be assigned per day using a single thermal cycler. Using the FCTRX sequences to design oligonucleotide primers, sub-localization can be achieved with panels of fragments from specific chromosomes.

Fluorescence *in situ* hybridization (FISH) of a DNA sequence to a metaphase chromosomal spread can further be used to provide a precise chromosomal location in one step. Chromosome spreads can be made using cells whose division has been blocked in metaphase by a chemical like colcemid that disrupts the mitotic spindle. The chromosomes can be treated briefly with trypsin, and then stained with Giemsa. A pattern of light and dark bands develops on each chromosome, so that the chromosomes can be identified individually. The FISH technique can be used with a DNA sequence as short as 500 or 600 bases. However, clones larger than 1,000 bases have a higher likelihood of binding to a unique chromosomal location with sufficient signal intensity for simple detection. Preferably 1,000 bases, and more preferably 2,000 bases, will suffice to get good results at a reasonable amount of time. For a review of this technique, *see,* Verma, *et al.*, HUMAN CHROMOSOMES: A MANUAL OF BASIC TECHNIQUES (Pergamon Press, New York 1988).

Reagents for chromosome mapping can be used individually to mark a single chromosome or a single site on that chromosome, or panels of reagents can be used for marking multiple sites and/or multiple chromosomes. Reagents corresponding to noncoding regions of the genes actually are preferred for mapping purposes. Coding sequences are more likely to be conserved within gene families, thus increasing the chance of cross hybridizations during chromosomal mapping.

Once a sequence has been mapped to a precise chromosomal location, the physical position of the sequence on the chromosome can be correlated with genetic map data. Such data are found, *e.g.,* in McKusick, MENDELIAN INHERITANCE IN MAN, available on-line through Johns Hopkins University Welch Medical Library). The relationship between genes and disease, mapped to the same chromosomal region, can then be identified through linkage analysis

(co-inheritance of physically adjacent genes), described in, *e.g.*, [redacted]land, *et al.*, 1987. *Nature*, 325: 783-787.

Moreover, differences in the DNA sequences between individuals affected and unaffected with a disease associated with the FCTRX gene, can be determined. If a mutation is observed in some or all of the affected individuals but not in any unaffected individuals, then the mutation is likely to be the causative agent of the particular disease. Comparison of affected and unaffected individuals generally involves first looking for structural alterations in the chromosomes, such as deletions or translocations that are visible from chromosome spreads or detectable using PCR based on that DNA sequence. Ultimately, complete sequencing of genes from several individuals can be performed to confirm the presence of a mutation and to distinguish mutations from polymorphisms.

Tissue Typing

The FCTRX sequences of the invention can also be used to identify individuals from minute biological samples. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identification. The sequences of the invention are useful as additional DNA markers for RFLP ("restriction fragment length polymorphisms," described in U.S. Patent No. 5,272,057).

Furthermore, the sequences of the invention can be used to provide an alternative technique that determines the actual base-by-base DNA sequence of selected portions of an individual's genome. Thus, the FCTRX sequences described herein can be used to prepare two PCR primers from the 5'- and 3'-termini of the sequences. These primers can then be used to amplify an individual's DNA and subsequently sequence it.

Panels of corresponding DNA sequences from individuals, prepared in this manner, can provide unique individual identifications, as each individual will have a unique set of such DNA sequences due to allelic differences. The sequences of the invention can be used to obtain such identification sequences from individuals and from tissue. The FCTRX sequences of the invention uniquely represent portions of the human genome. Allelic variation occurs to some degree in the coding regions of these sequences, and to a greater degree in the noncoding regions. It is estimated that allelic variation between individual humans occurs with a frequency of about once per each 500 bases. Much of the allelic variation is due to single nucleotide polymorphisms (SNPs), which include restriction fragment length polymorphisms (RFLPs).

Each of the sequences described herein can, to some degree, be used as a standard against which DNA from an individual can be compared for identification purposes. Because greater numbers of polymorphisms occur in the noncoding regions, fewer sequences are necessary to

differentiate individuals. The noncoding sequences can comfortably provide positive individual identification with a panel of perhaps 10 to 1,000 primers that each yield a noncoding amplified sequence of 100 bases. If predicted coding sequences, such as those in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, are used, a more appropriate number of primers for positive individual identification would be 500-2,000.

Predictive Medicine

The invention also pertains to the field of predictive medicine in which diagnostic assays, prognostic assays, pharmacogenomics, and monitoring clinical trials are used for prognostic (predictive) purposes to thereby treat an individual prophylactically. Accordingly, one aspect of the invention relates to diagnostic assays for determining FCTRX protein and/or nucleic acid expression as well as FCTRX activity, in the context of a biological sample (*e.g.*, blood, serum, cells, tissue) to thereby determine whether an individual is afflicted with a disease or disorder, or is at risk of developing a disorder, associated with aberrant FCTRX expression or activity. The disorders include Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital ceonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma , clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveilance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy -Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy. The invention also provides for prognostic

(or predictive) assays for determining whether an individual is at risk of developing a disorder associated with FCTRX protein, nucleic acid expression or activity. For example, mutations in an FCTRX gene can be assayed in a biological sample. Such assays can be used for prognostic or predictive purpose to thereby prophylactically treat an individual prior to the onset of a disorder characterized by or associated with FCTRX protein, nucleic acid expression, or biological activity.

Another aspect of the invention provides methods for determining FCTRX protein, nucleic acid expression or activity in an individual to thereby select appropriate therapeutic or prophylactic agents for that individual (referred to herein as "pharmacogenomics"). Pharmacogenomics allows for the selection of agents (*e.g.*, drugs) for therapeutic or prophylactic treatment of an individual based on the genotype of the individual (*e.g.*, the genotype of the individual examined to determine the ability of the individual to respond to a particular agent.)

Yet another aspect of the invention pertains to monitoring the influence of agents (*e.g.*, drugs, compounds) on the expression or activity of FCTRX in clinical trials.

These and other agents are described in further detail in the following sections.

Diagnostic Assays

An exemplary method for detecting the presence or absence of FCTRX in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting FCTRX protein or nucleic acid (*e.g.*, mRNA, genomic DNA) that encodes FCTRX protein such that the presence of FCTRX is detected in the biological sample. An agent for detecting FCTRX mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to FCTRX mRNA or genomic DNA. The nucleic acid probe can be, for example, a full-length FCTRX nucleic acid, such as the nucleic acid of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to FCTRX mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.

An agent for detecting FCTRX protein is an antibody capable of binding to FCTRX protein, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment thereof (*e.g.*, Fab or $F(ab')_2$) can be used. The term "labeled", with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (*i.e.*, physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include detection of a

primary antibody using a fluorescently-labeled secondary antibody and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently-labeled streptavidin. The term "biological sample" is intended to include tissues, cells and biological fluids isolated from a subject, as well as tissues, cells and fluids present within a subject. That is, the detection method of the invention can be used to detect FCTRX mRNA, protein, or genomic DNA in a biological sample *in vitro* as well as *in vivo*. For example, *in vitro* techniques for detection of FCTRX mRNA include Northern hybridizations and *in situ* hybridizations. *In vitro* techniques for detection of FCTRX protein include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations, and immunofluorescence. *In vitro* techniques for detection of FCTRX genomic DNA include Southern hybridizations. Furthermore, *in vivo* techniques for detection of FCTRX protein include introducing into a subject a labeled anti-FCTRX antibody. For example, the antibody can be labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

In one embodiment, the biological sample contains protein molecules from the test subject. Alternatively, the biological sample can contain mRNA molecules from the test subject or genomic DNA molecules from the test subject. A preferred biological sample is a peripheral blood leukocyte sample isolated by conventional means from a subject.

In another embodiment, the methods further involve obtaining a control biological sample from a control subject, contacting the control sample with a compound or agent capable of detecting FCTRX protein, mRNA, or genomic DNA, such that the presence of FCTRX protein, mRNA or genomic DNA is detected in the biological sample, and comparing the presence of FCTRX protein, mRNA or genomic DNA in the control sample with the presence of FCTRX protein, mRNA or genomic DNA in the test sample.

The invention also encompasses kits for detecting the presence of FCTRX in a biological sample. For example, the kit can comprise: a labeled compound or agent capable of detecting FCTRX protein or mRNA in a biological sample; means for determining the amount of FCTRX in the sample; and means for comparing the amount of FCTRX in the sample with a standard. The compound or agent can be packaged in a suitable container. The kit can further comprise instructions for using the kit to detect FCTRX protein or nucleic acid.

Prognostic Assays

The diagnostic methods described herein can furthermore be utilized to identify subjects having or at risk of developing a disease or disorder associated with aberrant FCTRX expression or activity. For example, the assays described herein, such as the preceding diagnostic assays or the following assays, can be utilized to identify a subject having or at risk of developing a

disorder associated with FCTRX protein, nucleic acid expression or activity. Alternatively, the prognostic assays can be utilized to identify a subject having or at risk for developing a disease or disorder. Thus, the invention provides a method for identifying a disease or disorder associated with aberrant FCTRX expression or activity in which a test sample is obtained from a subject and FCTRX protein or nucleic acid (*e.g.*, mRNA, genomic DNA) is detected, wherein the presence of FCTRX protein or nucleic acid is diagnostic for a subject having or at risk of developing a disease or disorder associated with aberrant FCTRX expression or activity. As used herein, a "test sample" refers to a biological sample obtained from a subject of interest. For example, a test sample can be a biological fluid (*e.g.*, serum), cell sample, or tissue.

Furthermore, the prognostic assays described herein can be used to determine whether a subject can be administered an agent (*e.g.*, an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate) to treat a disease or disorder associated with aberrant FCTRX expression or activity. For example, such methods can be used to determine whether a subject can be effectively treated with an agent for a disorder. Thus, the invention provides methods for determining whether a subject can be effectively treated with an agent for a disorder associated with aberrant FCTRX expression or activity in which a test sample is obtained and FCTRX protein or nucleic acid is detected (*e.g.*, wherein the presence of FCTRX protein or nucleic acid is diagnostic for a subject that can be administered the agent to treat a disorder associated with aberrant FCTRX expression or activity).

The methods of the invention can also be used to detect genetic lesions in an FCTRX gene, thereby determining if a subject with the lesioned gene is at risk for a disorder characterized by aberrant cell proliferation and/or differentiation. In various embodiments, the methods include detecting, in a sample of cells from the subject, the presence or absence of a genetic lesion characterized by at least one of an alteration affecting the integrity of a gene encoding an FCTRX-protein, or the misexpression of the FCTRX gene. For example, such genetic lesions can be detected by ascertaining the existence of at least one of: (*i*) a deletion of one or more nucleotides from an FCTRX gene; (*ii*) an addition of one or more nucleotides to an FCTRX gene; (*iii*) a substitution of one or more nucleotides of an FCTRX gene, (*iv*) a chromosomal rearrangement of an FCTRX gene; (*v*) an alteration in the level of a messenger RNA transcript of an FCTRX gene, (*vi*) aberrant modification of an FCTRX gene, such as of the methylation pattern of the genomic DNA, (*vii*) the presence of a non-wild-type splicing pattern of a messenger RNA transcript of an FCTRX gene, (*viii*) a non-wild-type level of an FCTRX protein, (*ix*) allelic loss of an FCTRX gene, and (*x*) inappropriate post-translational modification of an FCTRX protein. As described herein, there are a large number of assay techniques known

in the art which can be used for detecting lesions in an FCTRX gene. A preferred biological sample is a peripheral blood leukocyte sample isolated by conventional means from a subject. However, any biological sample containing nucleated cells may be used, including, for example, buccal mucosal cells.

In certain embodiments, detection of the lesion involves the use of a probe/primer in a polymerase chain reaction (PCR) (*see, e.g.*, U.S. Patent Nos. 4,683,195 and 4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligation chain reaction (LCR) (*see, e.g.*, Landegran, *et al.*, 1988. *Science* 241: 1077-1080; and Nakazawa, *et al.*, 1994. *Proc. Natl. Acad. Sci. USA* 91: 360-364), the latter of which can be particularly useful for detecting point mutations in the FCTRX-gene (*see,* Abravaya, *et al.*, 1995. *Nucl. Acids Res.* 23: 675-682). This method can include the steps of collecting a sample of cells from a patient, isolating nucleic acid (*e.g.*, genomic, mRNA or both) from the cells of the sample, contacting the nucleic acid sample with one or more primers that specifically hybridize to an FCTRX gene under conditions such that hybridization and amplification of the FCTRX gene (if present) occurs, and detecting the presence or absence of an amplification product, or detecting the size of the amplification product and comparing the length to a control sample. It is anticipated that PCR and/or LCR may be desirable to use as a preliminary amplification step in conjunction with any of the techniques used for detecting mutations described herein.

Alternative amplification methods include: self sustained sequence replication (*see,* Guatelli, *et al.*, 1990. *Proc. Natl. Acad. Sci. USA* 87: 1874-1878), transcriptional amplification system (*see,* Kwoh, *et al.*, 1989. *Proc. Natl. Acad. Sci. USA* 86: 1173-1177); Qβ Replicase (*see,* Lizardi, *et al*, 1988. *BioTechnology* 6: 1197), or any other nucleic acid amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection schemes are especially useful for the detection of nucleic acid molecules if such molecules are present in very low numbers.

In an alternative embodiment, mutations in an FCTRX gene from a sample cell can be identified by alterations in restriction enzyme cleavage patterns. For example, sample and control DNA is isolated, amplified (optionally), digested with one or more restriction endonucleases, and fragment length sizes are determined by gel electrophoresis and compared. Differences in fragment length sizes between sample and control DNA indicates mutations in the sample DNA. Moreover, the use of sequence specific ribozymes (*see, e.g.,* U.S. Patent No. 5,493,531) can be used to score for the presence of specific mutations by development or loss of a ribozyme cleavage site.

In other embodiments, genetic mutations in FCTRX can be identified by hybridizing a sample and control nucleic acids, *e.g.*, DNA or RNA, to high-density arrays containing hundreds or thousands of oligonucleotides probes. *See, e.g.,* Cronin, *et al.*, 1996. *Human Mutation* 7: 244-255; Kozal, *et al.*, 1996. *Nat. Med.* 2: 753-759. For example, genetic mutations in FCTRX can be identified in two dimensional arrays containing light-generated DNA probes as described in Cronin, *et al.*, *supra.* Briefly, a first hybridization array of probes can be used to scan through long stretches of DNA in a sample and control to identify base changes between the sequences by making linear arrays of sequential overlapping probes. This step allows the identification of point mutations. This is followed by a second hybridization array that allows the characterization of specific mutations by using smaller, specialized probe arrays complementary to all variants or mutations detected. Each mutation array is composed of parallel probe sets, one complementary to the wild-type gene and the other complementary to the mutant gene.

In yet another embodiment, any of a variety of sequencing reactions known in the art can be used to directly sequence the FCTRX gene and detect mutations by comparing the sequence of the sample FCTRX with the corresponding wild-type (control) sequence. Examples of sequencing reactions include those based on techniques developed by Maxim and Gilbert, 1977. *Proc. Natl. Acad. Sci. USA* 74: 560 or Sanger, 1977. *Proc. Natl. Acad. Sci. USA* 74: 5463. It is also contemplated that any of a variety of automated sequencing procedures can be utilized when performing the diagnostic assays (*see, e.g.,* Naeve, *et al.*, 1995. *Biotechniques* 19: 448), including sequencing by mass spectrometry (see, *e.g.*, PCT International Publication No. WO 94/16101; Cohen, *et al.*, 1996. *Adv. Chromatography* 36: 127-162; and Griffin, *et al.*, 1993. *Appl. Biochem. Biotechnol.* 38: 147-159).

Other methods for detecting mutations in the FCTRX gene include methods in which protection from cleavage agents is used to detect mismatched bases in RNA/RNA or RNA/DNA heteroduplexes. *See, e.g.,* Myers, *et al.*, 1985. *Science* 230: 1242. In general, the art technique of "mismatch cleavage" starts by providing heteroduplexes of formed by hybridizing (labeled) RNA or DNA containing the wild-type FCTRX sequence with potentially mutant RNA or DNA obtained from a tissue sample. The double-stranded duplexes are treated with an agent that cleaves single-stranded regions of the duplex such as which will exist due to basepair mismatches between the control and sample strands. For instance, RNA/DNA duplexes can be treated with RNase and DNA/DNA hybrids treated with S_1 nuclease to enzymatically digesting the mismatched regions. In other embodiments, either DNA/DNA or RNA/DNA duplexes can be treated with hydroxylamine or osmium tetroxide and with piperidine in order to digest mismatched regions. After digestion of the mismatched regions, the resulting material is then

separated by size on denaturing polyacrylamide gels to determine site of mutation. *See, e.g.,* Cotton, *et al.,* 1988. *Proc. Natl. Acad. Sci. USA* 85: 4397; Saleeba, *et al.,* 1992. *Methods Enzymol.* 217: 286-295. In an embodiment, the control DNA or RNA can be labeled for detection.

In still another embodiment, the mismatch cleavage reaction employs one or more proteins that recognize mismatched base pairs in double-stranded DNA (so called "DNA mismatch repair" enzymes) in defined systems for detecting and mapping point mutations in FCTRX cDNAs obtained from samples of cells. For example, the mutY enzyme of *E. coli* cleaves A at G/A mismatches and the thymidine DNA glycosylase from HeLa cells cleaves T at G/T mismatches. *See, e.g.,* Hsu, *et al.,* 1994. *Carcinogenesis* 15: 1657-1662. According to an exemplary embodiment, a probe based on an FCTRX sequence, *e.g.,* a wild-type FCTRX sequence, is hybridized to a cDNA or other DNA product from a test cell(s). The duplex is treated with a DNA mismatch repair enzyme, and the cleavage products, if any, can be detected from electrophoresis protocols or the like. *See, e.g.,* U.S. Patent No. 5,459,039.

In other embodiments, alterations in electrophoretic mobility will be used to identify mutations in FCTRX genes. For example, single strand conformation polymorphism (SSCP) may be used to detect differences in electrophoretic mobility between mutant and wild type nucleic acids. *See, e.g.,* Orita, *et al.,* 1989. *Proc. Natl. Acad. Sci. USA*: 86: 2766; Cotton, 1993. *Mutat. Res.* 285: 125-144; Hayashi, 1992. *Genet. Anal. Tech. Appl.* 9: 73-79. Single-stranded DNA fragments of sample and control FCTRX nucleic acids will be denatured and allowed to renature. The secondary structure of single-stranded nucleic acids varies according to sequence, the resulting alteration in electrophoretic mobility enables the detection of even a single base change. The DNA fragments may be labeled or detected with labeled probes. The sensitivity of the assay may be enhanced by using RNA (rather than DNA), in which the secondary structure is more sensitive to a change in sequence. In one embodiment, the subject method utilizes heteroduplex analysis to separate double stranded heteroduplex molecules on the basis of changes in electrophoretic mobility. *See, e.g.,* Keen, *et al.,* 1991. *Trends Genet.* 7: 5.

In yet another embodiment, the movement of mutant or wild-type fragments in polyacrylamide gels containing a gradient of denaturant is assayed using denaturing gradient gel electrophoresis (DGGE). *See, e.g.,* Myers, *et al.,* 1985. *Nature* 313: 495. When DGGE is used as the method of analysis, DNA will be modified to insure that it does not completely denature, for example by adding a GC clamp of approximately 40 bp of high-melting GC-rich DNA by PCR. In a further embodiment, a temperature gradient is used in place of a denaturing gradient

to identify differences in the mobility of control and sample DNA. *See, e.g.,* Rosenbaum and Reissner, 1987. *Biophys. Chem.* 265: 12753.

Examples of other techniques for detecting point mutations include, but are not limited to, selective oligonucleotide hybridization, selective amplification, or selective primer extension. For example, oligonucleotide primers may be prepared in which the known mutation is placed centrally and then hybridized to target DNA under conditions that permit hybridization only if a perfect match is found. *See, e.g.,* Saiki, *et al.*, 1986. *Nature* 324: 163; Saiki, *et al.*, 1989. *Proc. Natl. Acad. Sci. USA* 86: 6230. Such allele specific oligonucleotides are hybridized to PCR amplified target DNA or a number of different mutations when the oligonucleotides are attached to the hybridizing membrane and hybridized with labeled target DNA.

Alternatively, allele specific amplification technology that depends on selective PCR amplification may be used in conjunction with the instant invention. Oligonucleotides used as primers for specific amplification may carry the mutation of interest in the center of the molecule (so that amplification depends on differential hybridization; *see, e.g.,* Gibbs, *et al.*, 1989. *Nucl. Acids Res.* 17: 2437-2448) or at the extreme 3'-terminus of one primer where, under appropriate conditions, mismatch can prevent, or reduce polymerase extension (*see, e.g.,* Prossner, 1993. *Tibtech.* 11: 238). In addition it may be desirable to introduce a novel restriction site in the region of the mutation to create cleavage-based detection. *See, e.g.,* Gasparini, *et al.,* 1992. *Mol. Cell Probes* 6: 1. It is anticipated that in certain embodiments amplification may also be performed using *Taq* ligase for amplification. *See, e.g.,* Barany, 1991. *Proc. Natl. Acad. Sci. USA* 88: 189. In such cases, ligation will occur only if there is a perfect match at the 3'-terminus of the 5' sequence, making it possible to detect the presence of a known mutation at a specific site by looking for the presence or absence of amplification.

The methods described herein may be performed, for example, by utilizing pre-packaged diagnostic kits comprising at least one probe nucleic acid or antibody reagent described herein, which may be conveniently used, *e.g.*, in clinical settings to diagnose patients exhibiting symptoms or family history of a disease or illness involving an FCTRX gene.

Furthermore, any cell type or tissue, preferably peripheral blood leukocytes, in which FCTRX is expressed may be utilized in the prognostic assays described herein. However, any biological sample containing nucleated cells may be used, including, for example, buccal mucosal cells.

Pharmacogenomics

Agents, or modulators that have a stimulatory or inhibitory effect on FCTRX activity (*e.g.*, FCTRX gene expression), as identified by a screening assay described herein can be

administered to individuals to treat (prophylactically or therapeutically) disorders (The disorders include metabolic disorders, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital ceonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma , clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveilance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy -Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy) In conjunction with such treatment, the pharmacogenomics (*i.e.*, the study of the relationship between an individual's genotype and that individual's response to a foreign compound or drug) of the individual may be considered. Differences in metabolism of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, the pharmacogenomics of the individual permits the selection of effective agents (*e.g.*, drugs) for prophylactic or therapeutic treatments based on a consideration of the individual's genotype. Such pharmacogenomics can further be used to determine appropriate dosages and therapeutic regimens. Accordingly, the activity of FCTRX protein, expression of FCTRX nucleic acid, or mutation content of FCTRX genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual.

Pharmacogenomics deals with clinically significant hereditary variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. See *e.g.*,

Eichelbaum, 1996. *Clin. Exp. Pharmacol. Physiol.*, 23: 983-985; Linder, 1997. *Clin. Chem.*, 43: 254-266. In general, two types of pharmacogenetic conditions can be differentiated. Genetic conditions transmitted as a single factor altering the way drugs act on the body (altered drug action) or genetic conditions transmitted as single factors altering the way the body acts on drugs (altered drug metabolism). These pharmacogenetic conditions can occur either as rare defects or as polymorphisms. For example, glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common inherited enzymopathy in which the main clinical complication is hemolysis after ingestion of oxidant drugs (anti-malarials, sulfonamides, analgesics, nitrofurans) and consumption of fava beans.

As an illustrative embodiment, the activity of drug metabolizing enzymes is a major determinant of both the intensity and duration of drug action. The discovery of genetic polymorphisms of drug metabolizing enzymes (*e.g.*, N-acetyltransferase 2 (NAT 2) and cytochrome P450 enzymes CYP2D6 and CYP2C19) has provided an explanation as to why some patients do not obtain the expected drug effects or show exaggerated drug response and serious toxicity after taking the standard and safe dose of a drug. These polymorphisms are expressed in two phenotypes in the population, the extensive metabolizer (EM) and poor metabolizer (PM). The prevalence of PM is different among different populations. For example, the gene coding for CYP2D6 is highly polymorphic and several mutations have been identified in PM, which all lead to the absence of functional CYP2D6. Poor metabolizers of CYP2D6 and CYP2C19 quite frequently experience exaggerated drug response and side effects when they receive standard doses. If a metabolite is the active therapeutic moiety, PM show no therapeutic response, as demonstrated for the analgesic effect of codeine mediated by its CYP2D6-formed metabolite morphine. At the other extreme are the so called ultra-rapid metabolizers who do not respond to standard doses. Recently, the molecular basis of ultra-rapid metabolism has been identified to be due to CYP2D6 gene amplification.

Thus, the activity of FCTRX protein, expression of FCTRX nucleic acid, or mutation content of FCTRX genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual. In addition, pharmacogenetic studies can be used to apply genotyping of polymorphic alleles encoding drug-metabolizing enzymes to the identification of an individual's drug responsiveness phenotype. This knowledge, when applied to dosing or drug selection, can avoid adverse reactions or therapeutic failure and thus enhance therapeutic or prophylactic efficiency when treating a subject with an FCTRX modulator, such as a modulator identified by one of the exemplary screening assays described herein.

Monitoring of Effects During Clinical Trials

Monitoring the influence of agents (*e.g.*, drugs, compounds) on the expression or activity of FCTRX (*e.g.*, the ability to modulate aberrant cell proliferation and/or differentiation) can be applied not only in basic drug screening, but also in clinical trials. For example, the effectiveness of an agent determined by a screening assay as described herein to increase FCTRX gene expression, protein levels, or upregulate FCTRX activity, can be monitored in clinical trails of subjects exhibiting decreased FCTRX gene expression, protein levels, or downregulated FCTRX activity. Alternatively, the effectiveness of an agent determined by a screening assay to decrease FCTRX gene expression, protein levels, or downregulate FCTRX activity, can be monitored in clinical trails of subjects exhibiting increased FCTRX gene expression, protein levels, or upregulated FCTRX activity. In such clinical trials, the expression or activity of FCTRX and, preferably, other genes that have been implicated in, for example, a cellular proliferation or immune disorder can be used as a "read out" or markers of the immune responsiveness of a particular cell.

By way of example, and not of limitation, genes, including FCTRX, that are modulated in cells by treatment with an agent (*e.g.*, compound, drug or small molecule) that modulates FCTRX activity (*e.g.*, identified in a screening assay as described herein) can be identified. Thus, to study the effect of agents on cellular proliferation disorders, for example, in a clinical trial, cells can be isolated and RNA prepared and analyzed for the levels of expression of FCTRX and other genes implicated in the disorder. The levels of gene expression (*i.e.*, a gene expression pattern) can be quantified by Northern blot analysis or RT-PCR, as described herein, or alternatively by measuring the amount of protein produced, by one of the methods as described herein, or by measuring the levels of activity of FCTRX or other genes. In this manner, the gene expression pattern can serve as a marker, indicative of the physiological response of the cells to the agent. Accordingly, this response state may be determined before, and at various points during, treatment of the individual with the agent.

In one embodiment, the invention provides a method for monitoring the effectiveness of treatment of a subject with an agent (*e.g.*, an agonist, antagonist, protein, peptide, peptidomimetic, nucleic acid, small molecule, or other drug candidate identified by the screening assays described herein) comprising the steps of (*i*) obtaining a pre-administration sample from a subject prior to administration of the agent; (*ii*) detecting the level of expression of an FCTRX protein, mRNA, or genomic DNA in the preadministration sample; (*iii*) obtaining one or more post-administration samples from the subject; (*iv*) detecting the level of expression or activity of the FCTRX protein, mRNA, or genomic DNA in the post-administration samples; (*v*) comparing

the level of expression or activity of the FCTRX protein, mRN genomic DNA in the pre-administration sample with the FCTRX protein, mRNA, or genomic DNA in the post administration sample or samples; and (*vi*) altering the administration of the agent to the subject accordingly. For example, increased administration of the agent may be desirable to increase the expression or activity of FCTRX to higher levels than detected, *i.e.*, to increase the effectiveness of the agent. Alternatively, decreased administration of the agent may be desirable to decrease expression or activity of FCTRX to lower levels than detected, *i.e.*, to decrease the effectiveness of the agent.

Methods of Treatment

The invention provides for both prophylactic and therapeutic methods of treating a subject at risk of (or susceptible to) a disorder or having a disorder associated with aberrant FCTRX expression or activity. The disorders include cardiomyopathy, atherosclerosis, hypertension, congenital heart defects, aortic stenosis, atrial septal defect (ASD), atrioventricular (A-V) canal defect, ductus arteriosus, pulmonary stenosis, subaortic stenosis, ventricular septal defect (VSD), valve diseases, tuberous sclerosis, scleroderma, obesity, transplantation, adrenoleukodystrophy, congenital adrenal hyperplasia, prostate cancer, neoplasm; adenocarcinoma, lymphoma, uterus cancer, fertility, hemophilia, hypercoagulation, idiopathic thrombocytopenic purpura, immunodeficiencies, graft versus host disease, AIDS, bronchial asthma, Crohn's disease; multiple sclerosis, treatment of Albright Hereditary Ostoeodystrophy, and other diseases, disorders and conditions of the like.

These methods of treatment will be discussed more fully, below.

Disease and Disorders

Diseases and disorders that are characterized by increased (relative to a subject not suffering from the disease or disorder) levels or biological activity may be treated with Therapeutics that antagonize (*i.e.*, reduce or inhibit) activity. Therapeutics that antagonize activity may be administered in a therapeutic or prophylactic manner. Therapeutics that may be utilized include, but are not limited to: (*i*) an aforementioned peptide, or analogs, derivatives, fragments or homologs thereof; (*ii*) antibodies to an aforementioned peptide; (*iii*) nucleic acids encoding an aforementioned peptide; (*iv*) administration of antisense nucleic acid and nucleic acids that are "dysfunctional" (*i.e.*, due to a heterologous insertion within the coding sequences of coding sequences to an aforementioned peptide) that are utilized to "knockout" endoggenous function of an aforementioned peptide by homologous recombination (*see, e.g.*, Capecchi, 1989. *Science* 244: 1288-1292); or (*v*) modulators (*i.e.*, inhibitors, agonists and antagonists, including

additional peptide mimetic of the invention or antibodies specific to a peptide of the invention) that alter the interaction between an aforementioned peptide and its binding partner.

Diseases and disorders that are characterized by decreased (relative to a subject not suffering from the disease or disorder) levels or biological activity may be treated with Therapeutics that increase (*i.e.*, are agonists to) activity. Therapeutics that upregulate activity may be administered in a therapeutic or prophylactic manner. Therapeutics that may be utilized include, but are not limited to, an aforementioned peptide, or analogs, derivatives, fragments or homologs thereof; or an agonist that increases bioavailability.

Increased or decreased levels can be readily detected by quantifying peptide and/or RNA, by obtaining a patient tissue sample (*e.g.*, from biopsy tissue) and assaying it *in vitro* for RNA or peptide levels, structure and/or activity of the expressed peptides (or mRNAs of an aforementioned peptide). Methods that are well-known within the art include, but are not limited to, immunoassays (*e.g.*, by Western blot analysis, immunoprecipitation followed by sodium dodecyl sulfate (SDS) polyacrylamide gel electrophoresis, immunocytochemistry, etc.) and/or hybridization assays to detect expression of mRNAs (*e.g.*, Northern assays, dot blots, *in situ* hybridization, and the like).

Prophylactic Methods

In one aspect, the invention provides a method for preventing, in a subject, a disease or condition associated with an aberrant FCTRX expression or activity, by administering to the subject an agent that modulates FCTRX expression or at least one FCTRX activity. Subjects at risk for a disease that is caused or contributed to by aberrant FCTRX expression or activity can be identified by, for example, any or a combination of diagnostic or prognostic assays as described herein. Administration of a prophylactic agent can occur prior to the manifestation of symptoms characteristic of the FCTRX aberrancy, such that a disease or disorder is prevented or, alternatively, delayed in its progression. Depending upon the type of FCTRX aberrancy, for example, an FCTRX agonist or FCTRX antagonist agent can be used for treating the subject. The appropriate agent can be determined based on screening assays described herein. The prophylactic methods of the invention are further discussed in the following subsections.

Therapeutic Methods

Another aspect of the invention pertains to methods of modulating FCTRX expression or activity for therapeutic purposes. The modulatory method of the invention involves contacting a cell with an agent that modulates one or more of the activities of FCTRX protein activity associated with the cell. An agent that modulates FCTRX protein activity can be an agent as described herein, such as a nucleic acid or a protein, a naturally-occurring cognate ligand of an

FCTRX protein, a peptide, an FCTRX peptidomimetic, or other small molecule. In one embodiment, the agent stimulates one or more FCTRX protein activity. Examples of such stimulatory agents include active FCTRX protein and a nucleic acid molecule encoding FCTRX that has been introduced into the cell. In another embodiment, the agent inhibits one or more FCTRX protein activity. Examples of such inhibitory agents include antisense FCTRX nucleic acid molecules and anti-FCTRX antibodies. These modulatory methods can be performed *in vitro* (*e.g.*, by culturing the cell with the agent) or, alternatively, *in vivo* (*e.g.*, by administering the agent to a subject). As such, the invention provides methods of treating an individual afflicted with a disease or disorder characterized by aberrant expression or activity of an FCTRX protein or nucleic acid molecule. In one embodiment, the method involves administering an agent (*e.g.*, an agent identified by a screening assay described herein), or combination of agents that modulates (*e.g.*, up-regulates or down-regulates) FCTRX expression or activity. In another embodiment, the method involves administering an FCTRX protein or nucleic acid molecule as therapy to compensate for reduced or aberrant FCTRX expression or activity.

Stimulation of FCTRX activity is desirable in situations in which FCTRX is abnormally downregulated and/or in which increased FCTRX activity is likely to have a beneficial effect. One example of such a situation is where a subject has a disorder characterized by aberrant cell proliferation and/or differentiation (*e.g.*, cancer or immune associated disorders). Another example of such a situation is where the subject has a gestational disease (*e.g.*, preclampsia).

Determination of the Biological Effect of the Therapeutic

In various embodiments of the invention, suitable *in vitro* or *in vivo* assays are performed to determine the effect of a specific Therapeutic and whether its administration is indicated for treatment of the affected tissue.

In various specific embodiments, *in vitro* assays may be performed with representative cells of the type(s) involved in the patient's disorder, to determine if a given Therapeutic exerts the desired effect upon the cell type(s). Compounds for use in therapy may be tested in suitable animal model systems including, but not limited to rats, mice, chicken, cows, monkeys, rabbits, and the like, prior to testing in human subjects. Similarly, for *in vivo* testing, any of the animal model system known in the art may be used prior to administration to human subjects.

Prophylactic and Therapeutic Uses of the Compositions of the Invention

The FCTRX nucleic acids and proteins of the invention are useful in potential prophylactic and therapeutic applications implicated in a variety of disorders including, but not limited to: Also within the scope of the invention is the use of a Therapeutic in the manufacture

of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital ceonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma , clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveilance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy -Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy.

As an example, a cDNA encoding the FCTRX protein of the invention may be useful in gene therapy, and the protein may be useful when administered to a subject in need thereof. By way of non-limiting example, the compositions of the invention will have efficacy for treatment of patients suffering from: Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital ceonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma , clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways

resulting in tumor escape from immune surveilance, neurologic disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy -Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy.

Both the novel nucleic acid encoding the FCTRX protein, and the FCTRX protein of the invention, or fragments thereof, may also be useful in diagnostic applications, wherein the presence or amount of the nucleic acid or the protein are to be assessed. A further use could be as an anti-bacterial molecule (*i.e.*, some peptides have been found to possess anti-bacterial properties). These materials are further useful in the generation of antibodies which immunospecifically-bind to the novel substances of the invention for use in therapeutic or diagnostic methods.

EXAMPLES

The following examples illustrate by way of non-limiting example various aspects of the invention.

The following examples illustrate by way of non-limiting example various aspects of the invention.

Example 1: Method of Identifying the Nucleic Acids

The novel nucleic acids of the invention were identified by TblastN using a proprietary sequence file, run against the Genomic Daily Files made available by GenBank. The nucleic acids were further predicted by the proprietary software program GenScan™, including selection of exons. These were further modified by means of similarities using BLAST searches. The sequences were then manually corrected for apparent inconsistencies, thereby obtaining the sequences encoding the full-length proteins.

Example 2. Quantitative expression analysis of FCTR2 in various cells and tissues

The quantitative expression of various clones was assessed using microtiter plates containing RNA samples from a variety of normal and pathology-derived cells, cell lines and tissues using real time quantitative PCR (RTQ PCR; TAQMAN®). RTQ PCR was performed on a Perkin-Elmer Biosystems ABI PRISM® 7700 Sequence Detection System. Various collections of samples are assembled on the plates, and referred to as Panel 1 (containing cells and cell lines from normal and cancer sources), Panel 2 (containing samples derived from tissues, in particular from surgical samples, from normal and cancer sources), Panel 3 (containing samples derived from a wide variety of cancer sources) and Panel 4 (containing cells and cell lines from normal cells and cells related to inflammatory conditions).

First, the RNA samples were normalized to constitutively expressed genes such as β-actin and GAPDH. RNA (~50 ng total or ~1 ng polyA+) was converted to cDNA using the TAQMAN® Reverse Transcription Reagents Kit (PE Biosystems, Foster City, CA; Catalog No. N808-0234) and random hexamers according to the manufacturer's protocol. Reactions were performed in 20 ul and incubated for 30 min. at 48^{0}C. cDNA (5 ul) was then transferred to a separate plate for the TAQMAN® reaction using β-actin and GAPDH TAQMAN® Assay Reagents (PE Biosystems; Catalog Nos. 4310881E and 4310884E, respectively) and TAQMAN® universal PCR Master Mix (PE Biosystems; Catalog No. 4304447) according to the manufacturer's protocol. Reactions were performed in 25 ul using the following parameters: 2 min. at 50^{0}C; 10 min. at 95^{0}C; 15 sec. at 95^{0}C/1 min. at 60^{0}C (40 cycles). Results were recorded as CT values (cycle at which a given sample crosses a threshold level of fluorescence) using a log scale, with the difference in RNA concentration between a given sample and the sample with the lowest CT value being represented as 2 to the power of delta CT. The percent relative expression is then obtained by taking the reciprocal of this RNA difference and multiplying by 100. The average CT values obtained for ß-actin and GAPDH were used to normalize RNA samples. The RNA sample generating the highest CT value required no further diluting, while all other samples were diluted relative to this sample according to their β-actin /GAPDH average CT values.

Normalized RNA (5 ul) was converted to cDNA and analyzed via TAQMAN® using One Step RT-PCR Master Mix Reagents (PE Biosystems; Catalog No. 4309169) and gene-specific primers according to the manufacturer's instructions. Probes and primers were designed for each assay according to Perkin Elmer Biosystem's *Primer Express* Software package (version I for Apple Computer's Macintosh Power PC) or a similar algorithm using the target sequence as input. Default settings were used for reaction conditions and the following

parameters were set before selecting primers: primer concentration = 250 nM, primer melting temperature (T_m) range = 58°-60° C, primer optimal Tm = 59° C, maximum primer difference = 2° C, probe does not have 5' G, probe T_m must be 10° C greater than primer T_m, amplicon size 75 bp to 100 bp. The probes and primers selected (see below) were synthesized by Synthegen (Houston, TX, USA). Probes were double purified by HPLC to remove uncoupled dye and evaluated by mass spectroscopy to verify coupling of reporter and quencher dyes to the 5' and 3' ends of the probe, respectively. Their final concentrations were: forward and reverse primers, 900 nM each, and probe, 200nM.

PCR conditions: Normalized RNA from each tissue and each cell line was spotted in each well of a 96 well PCR plate (Perkin Elmer Biosystems). PCR cocktails including two probes (a probe specific for the target clone and another gene-specific probe multiplexed with the target probe) were set up using 1X TaqMan™ PCR Master Mix for the PE Biosystems 7700, with 5 mM MgCl2, dNTPs (dA, G, C, U at 1:1:1:2 ratios), 0.25 U/ml AmpliTaq Gold™ (PE Biosystems), and 0.4 U/μl RNase inhibitor, and 0.25 U/μl reverse transcriptase. Reverse transcription was performed at 48° C for 30 minutes followed by amplification/PCR cycles as follows: 95° C 10 min, then 40 cycles of 95° C for 15 seconds, 60° C for 1 minute.

In the results for Panel 1, the following abbreviations are used:

ca. = carcinoma,

* = established from metastasis,

met = metastasis,

s cell var= small cell variant,

non-s = non-sm =non-small,

squam = squamous,

pl. eff = pl effusion = pleural effusion,

glio = glioma,

astro = astrocytoma, and

neuro = neuroblastoma.

Panel 2

The plates for Panel 2 generally include 2 control wells and 94 test samples composed of RNA or cDNA isolated from human tissue procured by surgeons working in close cooperation

with the National Cancer Institute's Cooperative Human Tissue Network (CHTN) or the National Disease Research Initiative (NDRI). The tissues are derived from human malignancies and in cases where indicated many malignant tissues have "matched margins" obtained from noncancerous tissue just adjacent to the tumor. These are termed normal adjacent tissues and are denoted "NAT" in the results below. The tumor tissue and the "matched margins" are evaluated by two independent pathologists (the surgical pathologists and again by a pathologists at NDRI or CHTN). This analysis provides a gross histopathological assessment of tumor differentiation grade. Moreover, most samples include the original surgical pathology report that provides information regarding the clinical stage of the patient. These matched margins are taken from the tissue surrounding (i.e. immediately proximal) to the zone of surgery (designated "NAT", for normal adjacent tissue, in Table RR). In addition, RNA and cDNA samples were obtained from various human tissues derived from autopsies performed on elderly people or sudden death victims (accidents, etc.). These tissue were ascertained to be free of disease and were purchased from various commercial sources such as Clontech (Palo Alto, CA), Research Genetics, and Invitrogen.

RNA integrity from all samples is controlled for quality by visual assessment of agarose gel electropherograms using 28S and 18S ribosomal RNA staining intensity ratio as a guide (2:1 to 2.5:1 28s:18s) and the absence of low molecular weight RNAs that would be indicative of degradation products. Samples are controlled against genomic DNA contamination by RTQ PCR reactions run in the absence of reverse transcriptase using probe and primer sets designed to amplify across the span of a single exon.

Panel 4

Panel 4 includes samples on a 96 well plate (2 control wells, 94 test samples) composed of RNA (Panel 4r) or cDNA (Panel 4d) isolated from various human cell lines or tissues related to inflammatory conditions. Total RNA from control normal tissues such as colon and lung (Stratagene ,La Jolla, CA) and thymus and kidney (Clontech) were employed. Total RNA from liver tissue from cirrhosis patients and kidney from lupus patients was obtained from BioChain (Biochain Institute, Inc., Hayward, CA). Intestinal tissue for RNA preparation from patients diagnosed as having Crohn's disease and ulcerative colitis was obtained from the National Disease Research Interchange (NDRI) (Philadelphia, PA).

Astrocytes, lung fibroblasts, dermal fibroblasts, coronary artery smooth muscle cells, small airway epithelium, bronchial epithelium, microvascular dermal endothelial cells, microvascular lung endothelial cells, human pulmonary aortic endothelial cells, human umbilical vein endothelial cells were all purchased from Clonetics (Walkersville, MD) and grown in the media supplied for these cell types by Clonetics. These primary cell types were activated with various cytokines or combinations of cytokines for 6 and/or 12-14 hours, as indicated. The following cytokines were used; IL-1 beta at approximately 1-5 ng/ml, TNF alpha at approximately 5-10 ng/ml, IFN gamma at approximately 20-50 ng/ml, IL-4 at approximately 5-10 ng/ml, IL-9 at approximately 5-10 ng/ml, IL-13 at approximately 5-10 ng/ml. Endothelial cells were sometimes starved for various times by culture in the basal media from Clonetics with 0.1% serum.

Mononuclear cells were prepared from blood of employees at CuraGen Corporation, using Ficoll. LAK cells were prepared from these cells by culture in DMEM 5% FCS (Hyclone), 100 μM non essential amino acids (Gibco/Life Technologies, Rockville, MD), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5 x 10^{-5} M (Gibco), and 10 mM Hepes (Gibco) and Interleukin 2 for 4-6 days. Cells were then either activated with 10-20 ng/ml PMA and 1-2 μg/ml ionomycin, IL-12 at 5-10 ng/ml, IFN gamma at 20-50 ng/ml and IL-18 at 5-10 ng/ml for 6 hours. In some cases, mononuclear cells were cultured for 4-5 days in DMEM 5% FCS (Hyclone), 100 μM non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5 x 10^{-5} M (Gibco), and 10 mM Hepes (Gibco) with PHA (phytohemagglutinin) or PWM (pokeweed mitogen) at approximately 5 μg/ml. Samples were taken at 24, 48 and 72 hours for RNA preparation. MLR (mixed lymphocyte reaction) samples were obtained by taking blood from two donors, isolating the mononuclear cells using Ficoll and mixing the isolated mononuclear cells 1:1 at a final concentration of approximately $2x10^6$ cells/ml in DMEM 5% FCS (Hyclone), 100 μM non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol (5.5 x 10^{-5} M) (Gibco), and 10 mM Hepes (Gibco). The MLR was cultured and samples taken at various time points ranging from 1- 7 days for RNA preparation.

Monocytes were isolated from mononuclear cells using CD14 Miltenyi Beads, +ve VS selection columns and a Vario Magnet according to the manufacturer's instructions. Monocytes were differentiated into dendritic cells by culture in DMEM 5% fetal calf serum (FCS) (Hyclone, Logan, UT), 100 μM non essential amino acids (Gibco), 1 mM sodium pyruvate

(Gibco), mercaptoethanol 5.5 x 10^{-5} M (Gibco), and 10 mM Hepes (Gibco), 50 ng/ml GMCSF and 5 ng/ml IL-4 for 5-7 days. Macrophages were prepared by culture of monocytes for 5-7 days in DMEM 5% FCS (Hyclone), 100 μM non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5 x 10^{-5} M (Gibco), 10 mM Hepes (Gibco) and 10% AB Human Serum or MCSF at approximately 50 ng/ml. Monocytes, macrophages and dendritic cells were stimulated for 6 and 12-14 hours with lipopolysaccharide (LPS) at 100 ng/ml. Dendritic cells were also stimulated with anti-CD40 monoclonal antibody (Pharmingen) at 10 μg/ml for 6 and 12-14 hours.

CD4 lymphocytes, CD8 lymphocytes and NK cells were also isolated from mononuclear cells using CD4, CD8 and CD56 Miltenyi beads, positive VS selection columns and a Vario Magnet according to the manufacturer's instructions. CD45RA and CD45RO CD4 lymphocytes were isolated by depleting mononuclear cells of CD8, CD56, CD14 and CD19 cells using CD8, CD56, CD14 and CD19 Miltenyi beads and +ve selection. Then CD45RO beads were used to isolate the CD45RO CD4 lymphocytes with the remaining cells being CD45RA CD4 lymphocytes. CD45RA CD4, CD45RO CD4 and CD8 lymphocytes were placed in DMEM 5% FCS (Hyclone), 100 μM non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5 x 10^{-5} M (Gibco), and 10 mM Hepes (Gibco) and plated at 10^6 cells/ml onto Falcon 6 well tissue culture plates that had been coated overnight with 0.5 μg/ml anti-CD28 (Pharmingen) and 3 ug/ml anti-CD3 (OKT3, ATCC) in PBS. After 6 and 24 hours, the cells were harvested for RNA preparation. To prepare chronically activated CD8 lymphocytes, we activated the isolated CD8 lymphocytes for 4 days on anti-CD28 and anti-CD3 coated plates and then harvested the cells and expanded them in DMEM 5% FCS (Hyclone), 100 μM non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5 x 10^{-5} M (Gibco), and 10 mM Hepes (Gibco) and IL-2. The expanded CD8 cells were then activated again with plate bound anti-CD3 and anti-CD28 for 4 days and expanded as before. RNA was isolated 6 and 24 hours after the second activation and after 4 days of the second expansion culture. The isolated NK cells were cultured in DMEM 5% FCS (Hyclone), 100 μM non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5 x 10^{-5} M (Gibco), and 10 mM Hepes (Gibco) and IL-2 for 4-6 days before RNA was prepared.

To obtain B cells, tonsils were procured from NDRI. The tonsil was cut up with sterile dissecting scissors and then passed through a sieve. Tonsil cells were then spun down and resupended at 10^6 cells/ml in DMEM 5% FCS (Hyclone), 100 μM non essential amino acids

(Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5 ^{5} M (Gibco), and 10 mM Hepes (Gibco). To activate the cells, we used PWM at 5 μg/ml or anti-CD40 (Pharmingen) at approximately 10 μg/ml and IL-4 at 5-10 ng/ml. Cells were harvested for RNA preparation at 24,48 and 72 hours.

To prepare the primary and secondary Th1/Th2 and Tr1 cells, six-well Falcon plates were coated overnight with 10 μg/ml anti-CD28 (Pharmingen) and 2 μg/ml OKT3 (ATCC), and then washed twice with PBS. Umbilical cord blood CD4 lymphocytes (Poietic Systems, German Town, MD) were cultured at 10^{5}-10^{6} cells/ml in DMEM 5% FCS (Hyclone), 100 μM non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5 x 10^{-5} M (Gibco), 10 mM Hepes (Gibco) and IL-2 (4 ng/ml). IL-12 (5 ng/ml) and anti-IL4 (1 μg/ml) were used to direct to Th1, while IL-4 (5 ng/ml) and anti-IFN gamma (1 μg/ml) were used to direct to Th2 and IL-10 at 5 ng/ml was used to direct to Tr1. After 4-5 days, the activated Th1, Th2 and Tr1 lymphocytes were washed once in DMEM and expanded for 4-7 days in DMEM 5% FCS (Hyclone), 100 μM non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5 x 10^{-5} M (Gibco), 10 mM Hepes (Gibco) and IL-2 (1 ng/ml). Following this, the activated Th1, Th2 and Tr1 lymphocytes were re-stimulated for 5 days with anti-CD28/OKT3 and cytokines as described above, but with the addition of anti-CD95L (1 μg/ml) to prevent apoptosis. After 4-5 days, the Th1, Th2 and Tr1 lymphocytes were washed and then expanded again with IL-2 for 4-7 days. Activated Th1 and Th2 lymphocytes were maintained in this way for a maximum of three cycles. RNA was prepared from primary and secondary Th1, Th2 and Tr1 after 6 and 24 hours following the second and third activations with plate bound anti-CD3 and anti-CD28 mAbs and 4 days into the second and third expansion cultures in Interleukin 2.

The following leukocyte cells lines were obtained from the ATCC: Ramos, EOL-1, KU-812. EOL cells were further differentiated by culture in 0.1 mM dbcAMP at 5 x10^{5} cells/ml for 8 days, changing the media every 3 days and adjusting the cell concentration to 5 x10^{5} cells/ml. For the culture of these cells, we used DMEM or RPMI (as recommended by the ATCC), with the addition of 5% FCS (Hyclone), 100 μM non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5 x 10^{-5} M (Gibco), 10 mM Hepes (Gibco). RNA was either prepared from resting cells or cells activated with PMA at 10 ng/ml and ionomycin at 1 μg/ml for 6 and 14 hours. Keratinocyte line CCD106 and an airway epithelial tumor line NCI-

H292 were also obtained from the ATCC. Both were cultured in MEM 5% FCS (Hyclone), 100 µM non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5 x 10^{-5} M (Gibco), and 10 mM Hepes (Gibco). CCD1106 cells were activated for 6 and 14 hours with approximately 5 ng/ml TNF alpha and 1 ng/ml IL-1 beta, while NCI-H292 cells were activated for 6 and 14 hours with the following cytokines: 5 ng/ml IL-4, 5 ng/ml IL-9, 5 ng/ml IL-13 and 25 ng/ml IFN gamma.

For these cell lines and blood cells, RNA was prepared by lysing approximately 10^7 cells/ml using Trizol (Gibco BRL). Briefly, 1/10 volume of bromochloropropane (Molecular Research Corporation) was added to the RNA sample, vortexed and after 10 minutes at room temperature, the tubes were spun at 14,000 rpm in a Sorvall SS34 rotor. The aqueous phase was removed and placed in a 15 ml Falcon Tube. An equal volume of isopropanol was added and left at –20 degrees C overnight. The precipitated RNA was spun down at 9,000 rpm for 15 min in a Sorvall SS34 rotor and washed in 70% ethanol. The pellet was redissolved in 300 µl of RNAse-free water and 35 µl buffer (Promega) 5 µl DTT, 7 µl RNAsin and 8 µl DNAse were added. The tube was incubated at 37 degrees C for 30 minutes to remove contaminating genomic DNA, extracted once with phenol chloroform and re-precipitated with 1/10 volume of 3 M sodium acetate and 2 volumes of 100% ethanol. The RNA was spun down and placed in RNAse free water. RNA was stored at –80 degrees C.

The above detailed procedures were carried out to obtain the taqman profiles of the clones in question.

Given below are the Primers and the Taqman results for the following clones:

58092213.0.36 – Probe Name: Ag809 (Table 9 and Table 10)

29692275.0.1 – Probe Name: Ag2773 (Table 11 and Table 12)

32125243.0.21 – Probe Name: Ag427 (Table 13 and Table 14)

27455183.0.19 – Probe Name: Ag1541 (Table 15 and Table 16, 17, 18)

Table 8: Primer Design for Probe Ag809 (FCTR1)

Primer	Sequences	TM	Length	Start Po	SEQID NO
Forward	5'-ATGTGATCTTTGGCTGTGAAGT-3'	58.7	22	337	24
Probe	FAM-5'-CTACCCCATGGCCTCCATCGAGT-3'-TAMRA	69.4	23	365	25
Reverse		59.9	19	393	26

	5'-GGATGTCCAAGCCATCCTT-3'				

TABLE 9: TAQMAN RESULTS FOR FCTR1

Tissue_Name	Panel 1	Tissue_Name	Panel 2D	Tissue_Name	Panel 4D
Liver adenocarcinoma	79.6	Normal Colon GENPAK 061003	6.8	93768_Secondary Th1_anti-CD28/anti-CD3	2.0
Heart (fetal)	43.8	83219 CC Well to Mod Diff (ODO3866)	6.1	93769_Secondary Th2_anti-CD28/anti-CD3	1.5
Pancreas	2.1	83220 CC NAT (ODO3866)	2.5	93770_Secondary Tr1_anti-CD28/anti-CD3	2.5
Pancreatic ca. CAPAN 2	4.7	83221 CC Gr.2 rectosigmoid (ODO3868)	0.9	93573_Secondary Th1_resting day 4-6 in IL-2	1.0
Adrenal gland	2.3	83222 CC NAT (ODO3868)	1.2	93572_Secondary Th2_resting day 4-6 in IL-2	3.0
Thyroid	6.5	83235 CC Mod Diff (ODO3920)	3.8	93571_Secondary Tr1_resting day 4-6 in IL-2	1.7
Salivary gland	12.3	83236 CC NAT (ODO3920)	1.3	93568_primary Th1_anti-CD28/anti-CD3	0.4
Pituitary gland	8.7	83237 CC Gr.2 ascend colon (ODO3921)	6.9	93569_primary Th2_anti-CD28/anti-CD3	1.5
Brain (fetal)	0.0	83238 CC NAT (ODO3921)	4.0	93570_primary Tr1_anti-CD28/anti-CD3	2.0
Brain (whole)	3.0	83241 CC from Partial Hepatectomy (ODO4309)	1.2	93565_primary Th1_resting dy 4-6 in IL-2	5.4
Brain (amygdala)	2.4	83242 Liver NAT (ODO4309)	0.6	93566_primary Th2_resting dy 4-6 in IL-2	3.1
Brain (cerebellum)	0.0	87472 Colon mets to lung (OD04451-01)	4.4	93567_primary Tr1_resting dy 4-6 in IL-2	0.0
Brain (hippocampus)	13.0	87473 Lung NAT (OD04451-02)	1.2	93351_CD45RA CD4 lymphocyte_anti-CD28/anti-CD3	11.2
Brain (thalamus)	3.0	Normal Prostate Clontech A+ 6546-1	10.2	93352_CD45RO CD4 lymphocyte_anti-CD28/anti-CD3	1.2
Cerebral Cortex	2.3	84140 Prostate Cancer (OD04410)	41.8	93251_CD8 Lymphocytes_anti-CD28/anti-CD3	0.9
Spinal cord	2.6	84141 Prostate NAT (OD04410)	25.7	93353_chronic CD8 Lymphocytes 2ry_resting dy 4-6 in IL-2	0.0
CNS ca. (glio/astro) U87-MG	12.1	87073 Prostate Cancer (OD04720-01)	11.0	93574_chronic CD8 Lymphocytes 2ry_activated CD3/CD28	0.6
CNS ca. (glio/astro) U-118-MG	100.0	87074 Prostate NAT (OD04720-02)	10.0	93354_CD4_none	1.1
CNS ca. (astro) SW1783	6.5	Normal Lung GENPAK 061010	7.9	93252_Secondary Th1/Th2/Tr1_anti-CD95 CH11	0.0
CNS ca.* (neuro; met) SK-N-AS	52.1	83239 Lung Met to Muscle	6.5	93103_LAK cells_resting	0.5

		(ODO4286)			
CNS ca. (astro) SF-539	12.6	83240 Muscle NAT (ODO4286)	2.6	93788_LAK cells_IL-2	0.0
CNS ca. (astro) SNB-75	11.9	84136 Lung Malignant Cancer (OD03126)	14.8	93787_LAK cells_IL-2+IL-12	0.7
CNS ca. (glio)SNB-19	0.0	84137 Lung NAT (OD03126)	3.2	93789_LAK cells_IL-2+IFN gamma	1.1
CNS ca. (glio)U251	0.9	84871 Lung Cancer (OD04404)	2.1	93790_LAK cells_IL-2+ IL-18	0.3
CNS ca. (glio) SF-295	12.6	84872 Lung NAT (OD04404)	1.9	93104_LAK cells_PMA/ionomycin and IL-18	0.0
Heart	13.9	84875 Lung Cancer (OD04565)	0.3	93578_NK Cells IL-2_resting	1.3
Skeletal muscle	3.2	85950 Lung Cancer (OD04237-01)	1.3	93109_Mixed Lymphocyte Reaction_Two Way MLR	0.5
Bone marrow	3.6	85970 Lung NAT (OD04237-02)	2.6	93110_Mixed Lymphocyte Reaction_Two Way MLR	0.5
Thymus	4.2	83255 Ocular Mel Met to Liver (ODO4310)	0.1	93111_Mixed Lymphocyte Reaction_Two Way MLR	2.7
Spleen	61.6	83256 Liver NAT (ODO4310)	0.6	93112_Mononuclear Cells (PBMCs)_resting	0.0
Lymph node	3.3	84139 Melanoma Mets to Lung (OD04321)	2.5	93113_Mononuclear Cells (PBMCs)_PWM	1.3
Colorectal	11.9	84138 Lung NAT (OD04321)	2.6	93114_Mononuclear Cells (PBMCs)_PHA-L	1.0
Stomach	28.3	Normal Kidney GENPAK 061008	5.6	93249_Ramos (B cell)_none	1.2
Small intestine	4.5	83786 Kidney Ca, Nuclear grade 2 (OD04338)	0.6	93250_Ramos (B cell)_ionomycin	2.3
Colon ca. SW480	46.7	83787 Kidney NAT (OD04338)	3.7	93349_B lymphocytes_PWM	4.3
Colon ca.* (SW480 met)SW620	19.0	83788 Kidney Ca Nuclear grade 1/2 (OD04339)	0.8	93350_B lymphoytes_CD40L and IL-4	1.4
Colon ca. HT29	5.3	83789 Kidney NAT (OD04339)	3.1	92665_EOL-1 (Eosinophil)_dbcAMP differentiated	7.2
Colon ca. HCT-116	5.0	83790 Kidney Ca, Clear cell type (OD04340)	1.5	93248_EOL-1 (Eosinophil)_dbcAMP/PMAionomycin	3.0
Colon ca. CaCo-2	49.3	83791 Kidney NAT (OD04340)	5.1	93356_Dendritic Cells_none	1.5
83219 CC Well to Mod Diff (ODO3866)	3.0	83792 Kidney Ca, Nuclear grade 3 (OD04348)	14.5	93355_Dendritic Cells_LPS 100 ng/ml	0.7
Colon ca. HCC-2998	27.7	83793 Kidney NAT (OD04348)	2.5	93775_Dendritic Cells_anti-CD40	0.5
Gastric ca.* (liver met) NCI-N87	10.5	87474 Kidney Cancer	1.7	93774_Monocytes_resting	0.5

		(OD04622-01)			
Bladder	3.7	87475 Kidney NAT (OD04622-03)	2.0	93776_Monocytes_LPS 50 ng/ml	0.0
Trachea	23.5	85973 Kidney Cancer (OD04450-01)	0.3	93581_Macrophages_resting	1.3
Kidney	1.8	85974 Kidney NAT (OD04450-03)	2.0	93582_Macrophages_LPS 100 ng/ml	1.8
Kidney (fetal)	1.9	Kidney Cancer Clontech 8120607	7.0	93098_HUVEC (Endothelial)_none	2.3
Renal ca. 786-0	7.0	Kidney NAT Clontech 8120608	1.5	93099_HUVEC (Endothelial)_starved	9.0
Renal ca. A498	6.8	Kidney Cancer Clontech 8120613	2.0	93100_HUVEC (Endothelial)_IL-1b	1.2
Renal ca.RXF 393	4.7	Kidney NAT Clontech 8120614	4.1	93779_HUVEC (Endothelial)_IFN gamma	1.4
Renal ca.ACHN	9.8	Kidney Cancer Clontech 9010320	2.2	93102_HUVEC (Endothelial)_TNF alpha + IFN gamma	0.8
Renal ca.UO-31	1.3	Kidney NAT Clontech 9010321	3.5	93101_HUVEC (Endothelial)_TNF alpha + IL4	1.1
Renal ca.TK-10	0.6	Normal Uterus GENPAK 061018	3.1	93781_HUVEC (Endothelial)_IL-11	3.0
Liver	0.8	Uterus Cancer GENPAK 064011	17.6	93583_Lung Microvascular Endothelial Cells_none	0.8
Liver (fetal)	1.1	Normal Thyroid Clontech A+ 6570-1	3.7	93584_Lung Microvascular Endothelial Cells_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.5
Liver ca. (hepatoblast) HepG2	54.0	Thyroid Cancer GENPAK 064010	1.2	92662_Microvascular Dermal endothelium_none	1.1
Lung	3.9	Thyroid Cancer INVITROGEN A302152	0.6	92663_Microsvasular Dermal endothelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	1.0
Lung (fetal)	9.0	Thyroid NAT INVITROGEN A302153	2.6	93773_Bronchial epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml) **	0.0
Lung ca. (small cell) LX-1	34.4	Normal Breast GENPAK 061019	3.4	93347_Small Airway Epithelium_none	0.4
Lung ca. (small cell) NCI-H69	3.0	84877 Breast Cancer (OD04566)	0.9	93348_Small Airway Epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.5
Lung ca. (s.cell var.) SHP-77	13.0	85975 Breast Cancer (OD04590-01)	67.8	92668_Coronery Artery SMC_resting	5.8
Lung ca. (large cell)NCI-H460	6.8	85976 Breast Cancer Mets (OD04590-03)	51.1	92669_Coronery Artery SMC_TNFa (4 ng/ml) and IL1b (1 ng/ml)	2.3
Lung ca. (non-sm. cell) A549	3.4	87070 Breast Cancer Metastasis	12.7	93107_astrocytes_resting	2.7

		(OD04655-05)			
Lung ca. (non-s.cell) NCI-H23	34.4	GENPAK Breast Cancer 064006	8.9	93108_astr[redacted]es_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.0
Lung ca (non-s.cell) HOP-62	10.5	Breast Cancer Clontech 9100266	6.2	92666_KU-812 (Basophil)_resting	6.8
Lung ca. (non-s.cl) NCI-H522	47.6	Breast NAT Clontech 9100265	3.3	92667_KU-812 (Basophil)_PMA/ionoycin	8.4
Lung ca. (squam.) SW 900	4.7	Breast Cancer INVITROGEN A209073	3.4	93579_CCD1106 (Keratinocytes)_none	1.6
Lung ca. (squam.) NCI-H596	0.7	Breast NAT INVITROGEN A2090734	8.7	93580_CCD1106 (Keratinocytes)_TNFa and IFNg **	1.4
Mammary gland	9.9	Normal Liver GENPAK 061009	1.1	93791_Liver Cirrhosis	4.2
Breast ca.* (pl. effusion) MCF-7	5.6	Liver Cancer GENPAK 064003	0.6	93792_Lupus Kidney	1.9
Breast ca.* (pl.ef) MDA-MB-231	21.3	Liver Cancer Research Genetics RNA 1025	0.6	93577_NCI-H292	39.5
Breast ca.* (pl. effusion) T47D	66.0	Liver Cancer Research Genetics RNA 1026	1.4	93358_NCI-H292_IL-4	39.0
Breast ca. BT-549	7.6	Paired Liver Cancer Tissue Research Genetics RNA 6004-T	1.3	93360_NCI-H292_IL-9	65.5
Breast ca.MDA-N	18.7	Paired Liver Tissue Research Genetics RNA 6004-N	1.3	93359_NCI-H292_IL-13	37.1
Ovary	12.1	Paired Liver Cancer Tissue Research Genetics RNA 6005-T	1.1	93357_NCI-H292_IFN gamma	31.9
Ovarian ca.OVCAR-3	3.5	Paired Liver Tissue Research Genetics RNA 6005-N	0.3	93777_HPAEC_-	0.5
Ovarian ca.OVCAR-4	4.0	Normal Bladder GENPAK 061001	5.9	93778_HPAEC_IL-1 beta/TNA alpha	1.2
Ovarian ca. OVCAR-5	9.1	Bladder Cancer Research Genetics RNA 1023	1.7	93254_Normal Human Lung Fibroblast_none	42.3
Ovarian ca. OVCAR-8	12.7	Bladder Cancer INVITROGEN A302173	1.9	93253_Normal Human Lung Fibroblast_TNFa (4 ng/ml) and IL-1b (1 ng/ml)	17.8
Ovarian ca.IGROV-1	9.8	87071 Bladder Cancer (OD04718-01)	2.0	93257_Normal Human Lung Fibroblast_IL-4	100.0
Ovarian ca.*	0.4	87072 Bladder	3.3	93256_Normal Human Lung	72.7

(ascites) SK-OV-3		Normal Adjacent (OD04718-03)		Fibroblast_	
Uterus	6.9	Normal Ovary Res. Gen.	2.2	93255_Normal Human Lung Fibroblast_IL-13	60.7
Plancenta	4.6	Ovarian Cancer GENPAK 064008	29.1	93258_Normal Human Lung Fibroblast_IFN gamma	81.8
Prostate	15.7	87492 Ovary Cancer (OD04768-07)	100.0	93106_Dermal Fibroblasts CCD1070_resting	76.8
Prostate ca.* (bone met)PC-3	35.9	87493 Ovary NAT (OD04768-08)	2.2	93361_Dermal Fibroblasts CCD1070_TNF alpha 4 ng/ml	30.2
Testis	14.6	Normal Stomach GENPAK 061017	13.1	93105_Dermal Fibroblasts CCD1070_IL-1 beta 1 ng/ml	38.2
Melanoma Hs688(A).T	13.5	NAT Stomach Clontech 9060359	8.8	93772_dermal fibroblast_IFN gamma	34.2
Melanoma* (met) Hs688(B).T	71.2	Gastric Cancer Clontech 9060395	2.5	93771_dermal fibroblast_IL-4	80.7
Melanoma UACC-62	1.7	NAT Stomach Clontech 9060394	9.7	93259_IBD Colitis 1**	0.0
Melanoma M14	9.5	Gastric Cancer Clontech 9060397	15.9	93260_IBD Colitis 2	0.3
Melanoma LOX IMVI	2.4	NAT Stomach Clontech 9060396	12.9	93261_IBD Crohns	1.4
Melanoma* (met)SK-MEL-5	3.4	Gastric Cancer GENPAK 064005	12.1	735010_Colon_normal	35.6
Adipose	5.9			735019_Lung_none	11.0
				64028-1_Thymus_none	5.8
				64030-1_Kidney_none	9.7

Taqman results shown in Table 9 demonstrates that cFCTR1 is highly expressed by tumor cell lines and also overexpressed in tumor tissues, specifically breast and ovarian tumor compared to Normal Adjacent Tissues (NAT). There are reports that follistatin can act as a modulator of tumor growth and its expression also correlate with polycystic ovary syndrome, a benign form of ovarian tumor.

Table 10: Primer Design for Probe Ag2773 (FCTR4)

Primer	Sequences	TM	Length	Start Po	SEQ ID NO
Forward	5'-CCTTGCTTTGTCATATGCTGTT-3'	59.3	22	243	29
Probe	FAM-5'-CCCTTTGCCTGGAATATAAACTCTCA-3'-TAMRA	64.6	26	265	30
Reverse	5'-AGAGGAAGCTTTCTGGAGAAGA-3'	58.9	22	313	31

TABLE 11: TAQMAN RESULTS FOR GENE FCTR4

Tissue_Name	Panel 1D	Tissue_Name	Panel 2D	Tissue_Name	Panel 4D
Liver adenocarcinoma	18.3	Normal Colon GENPAK 061003	41.2	93768_Secondary Th1_anti-CD28/anti-CD3	12.7
Heart (fetal)	4.3	83219 CC Well to Mod Diff (ODO3866)	5.2	93769_Secondary Th2_anti-CD28/anti-CD3	14.2
Pancreas	3.1	83220 CC NAT (ODO3866)	2.5	93770_Secondary Tr1_anti-CD28/anti-CD3	14.7
Pancreatic ca.CAPAN 2	20.0	83221 CC Gr.2 rectosigmoid (ODO3868)	0.7	93573_Secondary Th1_resting day 4-6 in IL-2	4.7
Adrenal gland	7.4	83222 CC NAT (ODO3868)	1.4	93572_Secondary Th2_resting day 4-6 in IL-2	3.5
Thyroid	6.8	83235 CC Mod Diff (ODO3920)	14.0	93571_Secondary Tr1_resting day 4-6 in IL-2	7.0
Salivary gland	2.5	83236 CC NAT (ODO3920)	13.9	93568_primary Th1_anti-CD28/anti-CD3	22.4
Pituitary gland	5.7	83237 CC Gr.2 ascend colon (ODO3921)	16.2	93569_primary Th2_anti-CD28/anti-CD3	16.3
Brain (fetal)	14.4	83238 CC NAT (ODO3921)	5.2	93570_primary Tr1_anti-CD28/anti-CD3	21.8
Brain (whole)	19.6	83241 CC from Partial Hepatectomy (ODO4309)	13.9	93565_primary Th1_resting dy 4-6 in IL-2	30.2
Brain (amygdala)	3.7	83242 Liver NAT (ODO4309)	12.7	93566_primary Th2_resting dy 4-6 in IL-2	14.4
Brain (cerebellum)	2.1	87472 Colon mets to lung (OD04451-01)	3.4	93567_primary Tr1_resting dy 4-6 in IL-2	7.4
Brain (hippocampus)	22.7	87473 Lung NAT (OD04451-02)	1.5	93351_CD45RA CD4 lymphocyte_anti-CD28/anti-CD3	7.6
Brain (thalamus)	7.4	Normal Prostate Clontech A+ 6546-1	1.0	93352_CD45RO CD4 lymphocyte_anti-CD28/anti-CD3	11.1
Cerebral Cortex	47.3	84140 Prostate Cancer (OD04410)	3.1	93251_CD8 Lymphocytes_anti-CD28/anti-CD3	9.6
Spinal cord	8.3	84141 Prostate NAT (OD04410)	10.6	93353_chronic CD8 Lymphocytes 2ry_resting dy 4-6 in IL-2	9.7
CNS ca. (glio/astro)U87-MG	19.9	87073 Prostate Cancer (OD04720-01)	9.7	93574_chronic CD8 Lymphocytes 2ry_activated CD3/CD28	6.2
CNS ca. (glio/astro) U-118-MG	57.0	87074 Prostate NAT (OD04720-02)	8.3	93354_CD4_none	6.4
CNS ca. (astro) SW1783	10.0	Normal Lung GENPAK 061010	36.6	93252_Secondary Th1/Th2/Tr1_anti-CD95 CH11	9.3
CNS ca.* (neuro; met)SK-N-AS	44.8	83239 Lung Met to Muscle (ODO4286)	11.7	93103_LAK cells_resting	11.0
CNS ca. (astro) SF-539	37.4	83240 Muscle NAT (ODO4286)	3.4	93788_LAK cells_IL-2	10.4
CNS ca. (astro) SNB-75	62.0	84136 Lung Malignant Cancer (OD03126)	15.1	93787_LAK cells_IL-2+IL-12	7.4

CNS ca. (glio) SNB-19	24.8	84137 Lung NAT (OD03126)	17.4	93789_LAK c[redacted]IL-2+IFN gamma	11.6
CNS ca. (glio) U251	40.3	84871 Lung Cancer (OD04404)	5.0	93790_LAK cells_IL-2+ IL-18	13.3
CNS ca. (glio) SF-295	100.0	84872 Lung NAT (OD04404)	6.3	93104_LAK cells_PMA/ionomycin and IL-18	4.8
Heart	0.0	84875 Lung Cancer (OD04565)	3.2	93578_NK Cells IL-2_resting	6.2
Skeletal muscle	0.0	85950 Lung Cancer (OD04237-01)	15.8	93109_Mixed Lymphocyte Reaction_Two Way MLR	12.3
Bone marrow	33.7	85970 Lung NAT (OD04237-02)	10.5	93110_Mixed Lymphocyte Reaction_Two Way MLR	8.7
Thymus	12.4	83255 Ocular Mel Met to Liver (ODO4310)	5.9	93111_Mixed Lymphocyte Reaction_Two Way MLR	3.5
Spleen	21.3	83256 Liver NAT (ODO4310)	3.6	93112_Mononuclear Cells (PBMCs)_resting	4.5
Lymph node	13.4	84139 Melanoma Mets to Lung (OD04321)	10.6	93113_Mononuclear Cells (PBMCs)_PWM	21.2
Colorectal	38.2	84138 Lung NAT (OD04321)	10.6	93114_Mononuclear Cells (PBMCs)_PHA-L	8.9
Stomach	9.9	Normal Kidney GENPAK 061008	26.2	93249_Ramos (B cell)_none	100.0
Small intestine	17.9	83786 Kidney Ca, Nuclear grade 2 (OD04338)	22.2	93250_Ramos (B cell)_ionomycin	28.7
Colon ca.SW480	27.7	83787 Kidney NAT (OD04338)	11.7	93349_B lymphocytes_PWM	20.0
Colon ca.* (SW480 met)SW620	30.8	83788 Kidney Ca Nuclear grade 1/2 (OD04339)	45.1	93350_B lymphoytes_CD40L and IL-4	7.8
Colon ca.HT29	8.1	83789 Kidney NAT (OD04339)	14.8	92665_EOL-1 (Eosinophil)_dbcAMP differentiated	8.0
Colon ca.HCT-116	35.4	83790 Kidney Ca, Clear cell type (OD04340)	26.6	93248_EOL-1 (Eosinophil)_dbcAMP/PMAionomycin	3.8
Colon ca. CaCo-2	37.6	83791 Kidney NAT (OD04340)	10.4	93356_Dendritic Cells_none	6.8
83219 CC Well to Mod Diff (ODO3866)	17.8	83792 Kidney Ca, Nuclear grade 3 (OD04348)	2.4	93355_Dendritic Cells_LPS 100 ng/ml	3.3
Colon ca.HCC-2998	19.9	83793 Kidney NAT (OD04348)	18.8	93775_Dendritic Cells_anti-CD40	6.3
Gastric ca.* (liver met) NCI-N87	73.2	87474 Kidney Cancer (OD04622-01)	5.6	93774_Monocytes_resting	10.6
Bladder	43.2	87475 Kidney NAT (OD04622-03)	0.5	93776_Monocytes_LPS 50 ng/ml	3.5
Trachea	10.3	85973 Kidney Cancer (OD04450-01)	21.2	93581_Macrophages_resting	7.6
Kidney	9.2	85974 Kidney NAT (OD04450-03)	9.3	93582_Macrophages_LPS 100 ng/ml	3.9

Kidney (fetal)	0.0	Kidney Cancer [redacted]tech 8120607	0.0	93098_HUVEC (Endothelial)_none	8.5
Renal ca.786-0	53.6	Kidney NAT Clontech 8120608	0.9	93099_HUVEC (Endothelial)_starved	17.9
Renal ca. A498	36.1	Kidney Cancer Clontech 8120613	0.0	93100_HUVEC (Endothelial)_IL-1b	6.0
Renal ca.RXF 393	31.6	Kidney NAT Clontech 8120614	0.9	93779_HUVEC (Endothelial)_IFN gamma	7.8
Renal ca.ACHN	21.6	Kidney Cancer Clontech 9010320	2.7	93102_HUVEC (Endothelial)_TNF alpha + IFN gamma	5.7
Renal ca.UO-31	28.7	Kidney NAT Clontech 9010321	5.0	93101_HUVEC (Endothelial)_TNF alpha + IL4	5.6
Renal ca.TK-10	7.0	Normal Uterus GENPAK 061018	5.3	93781_HUVEC (Endothelial)_IL-11	4.9
Liver	14.2	Uterus Cancer GENPAK 064011	9.0	93583_Lung Microvascular Endothelial Cells_none	4.9
Liver (fetal)	14.5	Normal Thyroid Clontech A+ 6570-1	3.4	93584_Lung Microvascular Endothelial Cells_TNFa (4 ng/ml) and IL1b (1 ng/ml)	4.9
Liver ca. (hepatoblast) HepG2	59.9	Thyroid Cancer GENPAK 064010	1.8	92662_Microvascular Dermal endothelium_none	8.6
Lung	17.8	Thyroid Cancer INVITROGEN A302152	3.6	92663_Microsvasular Dermal endothelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	6.0
Lung (fetal)	9.6	Thyroid NAT INVITROGEN A302153	4.9	93773_Bronchial epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml) **	0.9
Lung ca. (small cell) LX-1	70.2	Normal Breast GENPAK 061019	8.5	93347_Small Airway Epithelium_none	1.3
Lung ca. (small cell) NCI-H69	29.9	84877 Breast Cancer (OD04566)	1.5	93348_Small Airway Epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	13.2
Lung ca. (s.cell var.) SHP-77	3.9	85975 Breast Cancer (OD04590-01)	23.8	92668_Coronery Artery SMC_resting	3.4
Lung ca. (large cell)NCI-H460	2.0	85976 Breast Cancer Mets (OD04590-03)	24.5	92669_Coronery Artery SMC_TNFa (4 ng/ml) and IL1b (1 ng/ml)	2.0
Lung ca. (non-sm. cell) A549	28.5	87070 Breast Cancer Metastasis (OD04655-05)	12.9	93107_astrocytes_resting	4.7
Lung ca. (non-s.cell) NCI-H23	36.1	GENPAK Breast Cancer 064006	11.8	93108_astrocytes_TNFa (4 ng/ml) and IL1b (1 ng/ml)	1.9
Lung ca (non-s.cell) HOP-62	29.9	Breast Cancer Clontech 9100266	3.2	92666_KU-812 (Basophil)_resting	5.8
Lung ca. (non-s.cl) NCI-H522	17.2	Breast NAT Clontech 9100265	1.8	92667_KU-812 (Basophil)_PMA/ionoycin	12.0
Lung ca. (squam.) SW 900	63.7	Breast Cancer INVITROGEN A209073	11.0	93579_CCD1106 (Keratinocytes)_none	4.9
Lung ca.	10.0	Breast NAT	7.1	93580_CCD1106	0.3

(squam.) NCI-H596		[redacted]VITROGEN [redacted]90734		(Keratinocyte [redacted]NFa and IFNg **	
Mammary gland	4.6	Normal Liver GENPAK 061009	8.8	93791_Liver Cirrhosis	1.8
Breast ca.* (pl. effusion) MCF-7	0.0	Liver Cancer GENPAK 064003	4.9	93792_Lupus Kidney	1.6
Breast ca.* (pl.ef) MDA-MB-231	38.7	Liver Cancer Research Genetics RNA 1025	1.0	93577_NCI-H292	11.1
Breast ca.* (pl. effusion) T47D	0.0	Liver Cancer Research Genetics RNA 1026	0.8	93358_NCI-H292_IL-4	12.2
Breast ca.BT-549	4.6	Paired Liver Cancer Tissue Research Genetics RNA 6004-T	3.0	93360_NCI-H292_IL-9	7.6
Breast ca.MDA-N	19.0	Paired Liver Tissue Research Genetics RNA 6004-N	7.3	93359_NCI-H292_IL-13	6.1
Ovary	1.7	Paired Liver Cancer Tissue Research Genetics RNA 6005-T	0.2	93357_NCI-H292_IFN gamma	5.8
Ovarian ca.OVCAR-3	4.8	Paired Liver Tissue Research Genetics RNA 6005-N	0.0	93777_HPAEC_-	6.8
Ovarian ca.OVCAR-4	0.0	Normal Bladder GENPAK 061001	19.8	93778_HPAEC_IL-1 beta/TNA alpha	5.4
Ovarian ca.OVCAR-5	39.0	Bladder Cancer Research Genetics RNA 1023	3.1	93254_Normal Human Lung Fibroblast_none	2.1
Ovarian ca.OVCAR-8	36.6	Bladder Cancer INVITROGEN A302173	9.9	93253_Normal Human Lung Fibroblast_TNFa (4 ng/ml) and IL-1b (1 ng/ml)	1.9
Ovarian ca.IGROV-1	0.0	87071 Bladder Cancer (OD04718-01)	6.6	93257_Normal Human Lung Fibroblast_IL-4	3.6
Ovarian ca.* (ascites) SK-OV-3	65.5	87072 Bladder Normal Adjacent (OD04718-03)	4.0	93256_Normal Human Lung Fibroblast_IL-9	3.3
Uterus	1.6	Normal Ovary Res. Gen.	0.3	93255_Normal Human Lung Fibroblast_IL-13	2.3
Plancenta	8.9	Ovarian Cancer GENPAK 064008	6.8	93258_Normal Human Lung Fibroblast_IFN gamma	2.9
Prostate	0.0	87492 Ovary Cancer (OD04768-07)	100.0	93106_Dermal Fibroblasts CCD1070_resting	5.6
Prostate ca.* (bone met)PC-3	9.2	87493 Ovary NAT (OD04768-08)	3.6	93361_Dermal Fibroblasts CCD1070_TNF alpha 4 ng/ml	17.4
Testis	29.5	Normal Stomach GENPAK 061017	8.6	93105_Dermal Fibroblasts CCD1070_IL-1 beta 1 ng/ml	3.8
Melanoma	14.3	NAT Stomach	0.7	93772_dermal fibroblast_IFN gamma	2.6

Hs688(A).T		Clontech 0359			
Melanoma* (met) Hs688(B).T	22.9	Gastric Cancer Clontech 9060395	3.9	93771_dermal fibroblast_IL-4	3.4
Melanoma UACC-62	9.7	NAT Stomach Clontech 9060394	5.3	93259_IBD Colitis 1**	0.2
Melanoma M14	12.7	Gastric Cancer Clontech 9060397	13.2	93260_IBD Colitis 2	0.4
Melanoma LOX IMVI	4.5	NAT Stomach Clontech 9060396	1.1	93261_IBD Crohns	0.3
Melanoma* (met) SK-MEL-5	21.8	Gastric Cancer GENPAK 064005	23.0	735010_Colon_normal	3.3
Adipose	6.7			735019_Lung_none	3.9
				64028-1_Thymus_none	7.7
				64030-1_Kidney_none	21.8

Table 12 shows the taqman results of clone FCTR4 indicating overexpression in ovarian cancer as compared to Normal Adjacent Tissue (NAT). In addition, increased expression is demonstrated by ovarian tumor cell line suggesting that antibodies could be used to treat ovarian tumors.

Table 13: Primer Design for Probe Ag427 (FCTR5)

Primer	Sequences	Length	Start Po	SEQ ID NO
Forward	5'-GAGCTACAGGCAGCCTCGAGT-3'	21	443	32
Probe	TET-5'-TGGCCCAGCTGACCCTGCTCA-3'-TAMRA	21		33
Reverse	5'-GGCTACGTCAGTGGGTTTGG-3'	20	449	34

Table 14: Taqman results for FCTR5

Tissue_Name	Panel 1	Tissue_Name	Panel 4D
Endothelial cells	10.7	93768_Secondary Th1_anti-CD28/anti-CD3	15.9
Endothelial cells (treated)	15.2	93769_Secondary Th2_anti-CD28/anti-CD3	14.7
Pancreas	16.2	93770_Secondary Tr1_anti-CD28/anti-CD3	21.9
Pancreatic ca.CAPAN 2	10.5	93573_Secondary Th1_resting day 4-6 in IL-2	12.3
Adipose	45.1	93572_Secondary Th2_resting day 4-6 in IL-2	16.2
Adrenal gland	61.6	93571_Secondary Tr1_resting day 4-6 in IL-2	16.2
Thyroid	13.1	93568_primary Th1_anti-CD28/anti-CD3	13.9

Salavary gland	33.7	93569_primary Th2_anti[redacted]8/anti-CD3	14.6
Pituitary gland	15.8	93570_primary Tr1_anti-[redacted]8/anti-CD3	26.2
Brain (fetal)	7.2	93565_primary Th1_resting dy 4-6 in IL-2	56.3
Brain (whole)	6.3	93566_primary Th2_resting dy 4-6 in IL-2	27.7
Brain (amygdala)	8.4	93567_primary Tr1_resting dy 4-6 in IL-2	31.6
Brain (cerebellum)	6.8	93351_CD45RA CD4 lymphocyte_anti-CD28/anti-CD3	12.1
Brain (hippocampus)	7.9	93352_CD45RO CD4 lymphocyte_anti-CD28/anti-CD3	17.1
Brain (substantia nigra)	9.5	93251_CD8 Lymphocytes_anti-CD28/anti-CD3	9.1
Brain (thalamus)	7.9	93353_chronic CD8 Lymphocytes 2ry_resting dy 4-6 in IL-2	13.4
Brain (hypothalamus)	23.0	93574_chronic CD8 Lymphocytes 2ry_activated CD3/CD28	9.2
Spinal cord	9.5	93354_CD4_none	7.6
CNS ca. (glio/astro)U87-MG	12.6	93252_Secondary Th1/Th2/Tr1_anti-CD95 CH11	20.2
CNS ca. (glio/astro)U-118-MG	11.6	93103_LAK cells_resting	57.0
CNS ca. (astro)SW1783	4.3	93788_LAK cells_IL-2	18.8
CNS ca.* (neuro; met)SK-N-AS	10.4	93787_LAK cells_IL-2+IL-12	14.2
CNS ca. (astro) SF-539	11.6	93789_LAK cells_IL-2+IFN gamma	20.9
CNS ca. (astro) SNB-75	4.4	93790_LAK cells_IL-2+ IL-18	14.8
CNS ca. (glio)SNB-19	31.6	93104_LAK cells_PMA/ionomycin and IL-18	12.9
CNS ca. (glio)U251	17.3	93578_NK Cells IL-2_resting	17.4
CNS ca. (glio)SF-295	20.9	93109_Mixed Lymphocyte Reaction_Two Way MLR	43.5
Heart	14.3	93110_Mixed Lymphocyte Reaction_Two Way MLR	19.3
Skeletal muscle	11.7	93111_Mixed Lymphocyte Reaction_Two Way MLR	12.6
Bone marrow	21.9	93112_Mononuclear Cells (PBMCs)_resting	8.7
Thymus	20.9	93113_Mononuclear Cells (PBMCs)_PWM	28.5
Spleen	23.8	93114_Mononuclear Cells (PBMCs)_PHA-L	26.2
Lymph node	24.2	93249_Ramos (B cell)_none	0.3
Colon (ascending)	17.2	93250_Ramos (B cell)_ionomycin	1.2
Stomach	11.1	93349_B lymphocytes_PWM	25.7
Small intestine	21.5	93350_B lymphoytes_CD40L and IL-4	13.0
Colon ca.SW480	12.2	92665_EOL-1 (Eosinophil)_dbcAMP differentiated	26.4
Colon ca.* (SW480 met)SW620	8.6	93248_EOL-1 (Eosinophil)_dbcAMP/PMAionomycin	11.4
Colon ca.HT29	16.2	93356_Dendritic Cells_none	40.3
Colon ca.HCT-116	8.1	93355_Dendritic Cells_LPS 100 ng/ml	33.0
Colon ca.CaCo-2	22.1	93775_Dendritic Cells_anti-CD40	20.5
Colon ca.HCT-15	18.6	93774_Monocytes_resting	23.3
Colon ca.HCC-2998	21.9	93776_Monocytes_LPS 50 ng/ml	6.9
Gastric ca.* (liver met) NCI-N87	42.9	93581_Macrophages_resting	14.7
Bladder	95.3	93582_Macrophages_LPS 100 ng/ml	64.6
Trachea	18.3	93098_HUVEC (Endothelial)_none	6.8
Kidney	25.7	93099_HUVEC (Endothelial)_starved	13.9
Kidney (fetal)	15.8	93100_HUVEC (Endothelial)_IL-1b	7.5
Renal ca.786-0	16.5	93779_HUVEC (Endothelial)_IFN gamma	27.7
Renal ca.A498	16.5	93102_HUVEC (Endothelial)_TNF alpha + IFN gamma	11.8
Renal ca.RXF 393	7.4	93101_HUVEC (Endothelial)_TNF alpha + IL4	6.7

Renal ca.ACHN	11.9	93781_HUVEC (Endothe IL-11	10.4
Renal ca.UO-31	15.8	93583_Lung Microvascu ndothelial Cells_none	8.8
Renal ca.TK-10	28.7	93584_Lung Microvascular Endothelial Cells_TNFa (4 ng/ml) and IL1b (1 ng/ml)	8.6
Liver	100.0	92662_Microvascular Dermal endothelium_none	22.1
Liver (fetal)	81.8	92663_Microsvasular Dermal endothelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	18.7
Liver ca. (hepatoblast) HepG2	28.3	93773_Bronchial epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml) **	35.4
Lung	10.7	93347_Small Airway Epithelium_none	10.9
Lung (fetal)	10.9	93348_Small Airway Epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	50.0
Lung ca. (small cell) LX-1	24.3	92668_Coronery Artery SMC_resting	27.9
Lung ca. (small cell) NCI-H69	41.5	92669_Coronery Artery SMC_TNFa (4 ng/ml) and IL1b (1 ng/ml)	25.4
Lung ca. (s.cell var.) SHP-77	4.6	93107_astrocytes_resting	7.4
Lung ca. (large cell)NCI-H460	46.3	93108_astrocytes_TNFa (4 ng/ml) and IL1b (1 ng/ml)	10.7
Lung ca. (non-sm. cell) A549	45.4	92666_KU-812 (Basophil)_resting	3.2
Lung ca. (non-s.cell) NCI-H23	54.3	92667_KU-812 (Basophil)_PMA/ionoycin	6.7
Lung ca (non-s.cell) HOP-62	50.7	93579_CCD1106 (Keratinocytes)_none	12.2
Lung ca. (non-s.cl) NCI-H522	38.4	93580_CCD1106 (Keratinocytes)_TNFa and IFNg **	100.0
Lung ca. (squam.) SW 900	30.8	93791_Liver Cirrhosis	27.6
Lung ca. (squam.) NCI-H596	15.5	93792_Lupus Kidney	32.3
Mammary gland	65.5	93577_NCI-H292	77.4
Breast ca.* (pl. effusion) MCF-7	4.4	93358_NCI-H292_IL-4	70.2
Breast ca.* (pl.ef) MDA-MB-231	3.5	93360_NCI-H292_IL-9	54.3
Breast ca.* (pl. effusion)T47D	8.7	93359_NCI-H292_IL-13	47.0
Breast ca. BT-549	5.7	93357_NCI-H292_IFN gamma	52.9
Breast ca.MDA-N	16.6	93777_HPAEC_-	23.8
Ovary	20.5	93778_HPAEC_IL-1 beta/TNA alpha	21.5
Ovarian ca. OVCAR-3	21.6	93254_Normal Human Lung Fibroblast_none	49.3
Ovarian ca.OVCAR-4	8.3	93253_Normal Human Lung Fibroblast_TNFa (4 ng/ml) and IL-1b (1 ng/ml)	40.3
Ovarian ca.OVCAR-5	26.1	93257_Normal Human Lung Fibroblast_IL-4	48.3
Ovarian ca.OVCAR-8	48.0	93256_Normal Human Lung Fibroblast_IL-9	29.3
Ovarian ca.IGROV-1	9.3	93255_Normal Human Lung Fibroblast_IL-13	73.7
Ovarian ca.* (ascites)SK-OV-3	8.8	93258_Normal Human Lung Fibroblast_IFN gamma	66.9
Uterus	13.4	93106_Dermal Fibroblasts CCD1070_resting	20.2
Plancenta	9.4	93361_Dermal Fibroblasts CCD1070_TNF alpha 4 ng/ml	35.1
Prostate	21.3	93105_Dermal Fibroblasts CCD1070_IL-1 beta 1 ng/ml	15.0
Prostate ca.* (bone met)PC-3	17.7	93772_dermal fibroblast_IFN gamma	21.8
Testis	11.7	93771_dermal fibroblast_IL-4	21.2
Melanoma Hs688(A).T	9.0	93259_IBD Colitis 1**	8.8
Melanoma* (met) Hs688(B).T	12.9	93260_IBD Colitis 2	3.5
Melanoma UACC-62	12.4	93261_IBD Crohns	1.3

Melanoma M14	9.5	735010_Colon_normal	20.3
Melanoma LOX IMVI	8.1	735019_Lung_none	40.3
Melanoma* (met) SK-MEL-5	8.8	64028-1_Thymus_none	33.5
Melanoma SK-MEL-28	8.0	64030-1_Kidney_none	21.0

Taqman results in Table 14 show high expression of clone FCTR5 in bladder, liver and adrenal gland suggesting a possible role in the treatment of diseases involving these tissues.

Table 15: Primer Design for Probe Ag1541 (FCTR6)

Primer	Sequences	TM	Length	Start Pos.	SEQ ID NO
Forward	5'-AGAAGAACACCCCAGGGATATA-3'	58.8	22	1076	35
Probe	FAM-5'-CCTCGTTGGTGAACTACAACCTCTGG-3'-TAMRA	67.9	26	1100	36
Reverse	5'-CCTCTAGCTGGGTCACTTTCTC-3'	59.5	22	1129	37

TABLE 16: TAQMAN RESULTS FOR FCTR6 (PANEL 1D)

Tissue_Name	Panel 1D Run 1	Panel 1D Run 2
Liver adenocarcinoma	0.0	0.0
Heart (fetal)	0.0	0.0
Pancreas	0.0	0.0
Pancreatic ca.CAPAN 2	0.0	0.0
Adrenal gland	0.0	0.0
Thyroid	0.0	0.0
Salivary gland	0.0	0.0
Pituitary gland	0.0	0.0
Brain (fetal)	0.5	0.4
Brain (whole)	1.1	1.7
Brain (amygdala)	0.0	1.8
Brain (cerebellum)	0.6	1.9
Brain (hippocampus)	3.3	3.4
Brain (thalamus)	1.0	1.2
Cerebral Cortex	1.6	2.6
Spinal cord	2.5	0.4
CNS ca. (glio/astro)U87-MG	0.0	0.0
CNS ca. (glio/astro)U-118-MG	0.0	0.0
CNS ca. (astro)SW1783	0.0	0.0
CNS ca.* (neuro; met)SK-N-AS	0.0	0.0
CNS ca. (astro)SF-539	0.0	0.0
CNS ca. (astro) SNB-75	0.7	0.0
CNS ca. (glio)SNB-19	0.0	0.0
CNS ca. (glio)U251	0.0	0.0
CNS ca. (glio)SF-295	0.0	0.8
Heart	0.0	0.0
Skeletal muscle	0.0	0.0

Bone marrow	[redacted]	0.0
Thymus	[redacted]	0.0
Spleen	0.0	0.0
Lymph node	0.0	0.0
Colorectal	0.0	0.6
Stomach	1.9	0.0
Small intestine	0.0	1.0
Colon ca. SW480	0.0	0.0
Colon ca.* (SW480 met)SW620	0.0	0.0
Colon ca. HT29	0.0	0.0
Colon ca. HCT-116	0.6	0.4
Colon ca.CaCo-2	1.5	0.0
83219 CC Well to Mod Diff (ODO3866)	0.0	0.0
Colon ca.HCC-2998	0.0	0.0
Gastric ca.* (liver met) NCI-N87	1.2	0.0
Bladder	0.0	0.0
Trachea	0.0	0.4
Kidney	0.8	1.2
Kidney (fetal)	0.5	0.7
Renal ca.786-0	0.0	0.0
Renal ca.A498	0.0	0.0
Renal ca.RXF 393	0.0	0.0
Renal ca.ACHN	0.0	0.0
Renal ca. UO-31	0.0	0.0
Renal ca.TK-10	0.0	0.0
Liver	0.0	0.0
Liver (fetal)	0.2	0.0
Liver ca. (hepatoblast) HepG2	0.0	0.0
Lung	0.0	0.0
Lung (fetal)	0.0	0.0
Lung ca. (small cell) LX-1	1.7	2.3
Lung ca. (small cell)NCI-H69	0.0	0.0
Lung ca. (s.cell var.) SHP-77	1.3	2.5
Lung ca. (large cell)NCI-H460	0.0	0.0
Lung ca. (non-sm. cell) A549	0.0	0.0
Lung ca. (non-s.cell) NCI-H23	1.2	0.4
Lung ca (non-s.cell) HOP-62	0.0	0.0
Lung ca. (non-s.cl) NCI-H522	0.0	0.0
Lung ca. (squam.) SW 900	0.0	0.7
Lung ca. (squam.) NCI-H596	0.0	1.3
Mammary gland	0.0	1.5
Breast ca.* (pl. effusion) MCF-7	0.0	0.0
Breast ca.* (pl.ef) MDA-MB-231	5.8	0.5
Breast ca.* (pl. effusion) T47D	1.2	0.3
Breast ca. BT-549	0.5	0.0
Breast ca. MDA-N	0.0	0.0
Ovary	0.0	0.0
Ovarian ca. OVCAR-3	0.0	0.0
Ovarian ca.OVCAR-4	0.0	0.0
Ovarian ca.OVCAR-5	3.6	0.7
Ovarian ca.OVCAR-8	0.0	0.0
Ovarian ca.IGROV-1	0.0	0.0
Ovarian ca.* (ascites) SK-OV-3	0.0	0.0
Uterus	0.0	0.0
Plancenta	0.0	0.0
Prostate	0.0	0.7
Prostate ca.* (bone met)PC-3	0.0	0.0
Testis	100.0	100.0
Melanoma Hs688(A).T	0.0	0.0

Melanoma* (met) Hs688(B).T	[redacted]	0.0
Melanoma UACC-62	[redacted]	0.0
Melanoma M14	0.0	0.0
Melanoma LOX IMVI	0.0	0.0
Melanoma* (met)SK-MEL-5	0.0	0.0
Adipose	0.5	0.0

Table 17: Taqman Results for FCTR6 (Panel 2D)

Tissue_Name	Panel 2D Run 1	Run 2
Normal Colon GENPAK 061003	5.4	2.4
83219 CC Well to Mod Diff (ODO3866)	7.3	0.0
83220 CC NAT (ODO3866)	5.8	1.5
83221 CC Gr.2 rectosigmoid (ODO3868)	3.4	0.0
83222 CC NAT (ODO3868)	0.0	0.0
83235 CC Mod Diff (ODO3920)	11.0	1.4
83236 CC NAT (ODO3920)	0.0	0.0
83237 CC Gr.2 ascend colon (ODO3921)	6.2	2.5
83238 CC NAT (ODO3921)	10.2	0.0
83241 CC from Partial Hepatectomy (ODO4309)	3.6	0.0
83242 Liver NAT (ODO4309)	0.0	2.4
87472 Colon mets to lung (OD04451-01)	7.2	4.4
87473 Lung NAT (OD04451-02)	0.0	0.0
Normal Prostate Clontech A+ 6546-1	4.8	2.9
84140 Prostate Cancer (OD04410)	3.5	0.0
84141 Prostate NAT (OD04410)	3.4	0.0
87073 Prostate Cancer (OD04720-01)	9.0	8.5
87074 Prostate NAT (OD04720-02)	0.0	0.0
Normal Lung GENPAK 061010	17.7	6.5
83239 Lung Met to Muscle (ODO4286)	0.0	2.3
83240 Muscle NAT (ODO4286)	0.0	0.0
84136 Lung Malignant Cancer (OD03126)	6.5	5.7
84137 Lung NAT (OD03126)	0.0	0.0
84871 Lung Cancer (OD04404)	0.0	0.0
84872 Lung NAT (OD04404)	0.0	0.0
84875 Lung Cancer (OD04565)	0.0	0.0
85950 Lung Cancer (OD04237-01)	0.0	0.0
85970 Lung NAT (OD04237-02)	0.0	0.0
83255 Ocular Mel Met to Liver (ODO4310)	4.3	0.0
83256 Liver NAT (ODO4310)	0.0	0.0
84139 Melanoma Mets to Lung (OD04321)	0.0	0.0
84138 Lung NAT (OD04321)	0.0	0.0
Normal Kidney GENPAK 061008	28.1	39.2
83786 Kidney Ca, Nuclear grade 2 (OD04338)	0.0	3.0
83787 Kidney NAT (OD04338)	22.7	31.6
83788 Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	3.1
83789 Kidney NAT (OD04339)	97.3	100.0
83790 Kidney Ca, Clear cell type (OD04340)	0.0	0.0
83791 Kidney NAT (OD04340)	100.0	34.4
83792 Kidney Ca, Nuclear grade 3 (OD04348)	2.0	4.9
83793 Kidney NAT (OD04348)	30.2	19.9
87474 Kidney Cancer (OD04622-01)	0.0	2.4
87475 Kidney NAT (OD04622-03)	8.4	7.2
85973 Kidney Cancer (OD04450-01)	0.0	0.0
85974 Kidney NAT (OD04450-03)	47.3	12.9

Kidney Cancer Clontech 8120607	[redacted]	0.0
Kidney NAT Clontech [redacted]608	[redacted]	0.0
Kidney Cancer Clontech 8120613	0.0	0.0
Kidney NAT Clontech 8120614	20.6	22.9
Kidney Cancer Clontech 9010320	0.0	0.0
Kidney NAT Clontech 9010321	3.4	26.4
Normal Uterus GENPAK 061018	0.0	0.0
Uterus Cancer GENPAK 064011	14.9	0.0
Normal Thyroid Clontech A+ 6570-1	0.0	0.0
Thyroid Cancer GENPAK 064010	0.0	0.0
Thyroid Cancer INVITROGEN A302152	0.0	0.0
Thyroid NAT INVITROGEN A302153	0.0	0.0
Normal Breast GENPAK 061019	5.2	3.5
84877 Breast Cancer (OD04566)	0.0	0.0
85975 Breast Cancer (OD04590-01)	0.0	0.0
85976 Breast Cancer Mets (OD04590-03)	0.0	0.0
87070 Breast Cancer Metastasis (OD04655-05)	0.0	0.0
GENPAK Breast Cancer 064006	0.0	2.5
Breast Cancer Clontech 9100266	6.2	0.0
Breast NAT Clontech 9100265	0.0	0.0
Breast Cancer INVITROGEN A209073	1.5	2.5
Breast NAT INVITROGEN A2090734	24.3	26.2
Normal Liver GENPAK 061009	10.5	2.7
Liver Cancer GENPAK 064003	5.9	1.7
Liver Cancer Research Genetics RNA 1025	21.6	11.0
Liver Cancer Research Genetics RNA 1026	0.0	0.0
Paired Liver Cancer Tissue Research Genetics RNA 6004-T	3.3	13.5
Paired Liver Tissue Research Genetics RNA 6004-N	3.2	1.4
Paired Liver Cancer Tissue Research Genetics RNA 6005-T	0.0	0.0
Paired Liver Tissue Research Genetics RNA 6005-N	0.0	0.0
Normal Bladder GENPAK 061001	0.0	0.0
Bladder Cancer Research Genetics RNA 1023	0.0	0.0
Bladder Cancer INVITROGEN A302173	4.6	2.3
87071 Bladder Cancer (OD04718-01)	17.9	11.4
87072 Bladder Normal Adjacent (OD04718-03)	0.0	0.0
Normal Ovary Res. Gen.	0.0	0.0
Ovarian Cancer GENPAK 064008	1.7	4.8
87492 Ovary Cancer (OD04768-07)	0.0	2.1
87493 Ovary NAT (OD04768-08)	0.0	0.0
Normal Stomach GENPAK 061017	3.3	2.9
NAT Stomach Clontech 9060359	0.0	0.0
Gastric Cancer Clontech 9060395	0.0	0.0
NAT Stomach Clontech 9060394	0.0	0.0
Gastric Cancer Clontech 9060397	0.0	0.0
NAT Stomach Clontech 9060396	0.0	0.0
Gastric Cancer GENPAK 064005	6.3	3.8

Table 18: Taqman Results for clone 27455183.0.19 (Panel 4D)

Tissue_Name	Panel 4D Run 1	Run 2
93768_Secondary Th1_anti-CD28/anti-CD3	0.0	0.0
93769_Secondary Th2_anti-CD28/anti-CD3	0.0	0.0
93770_Secondary Tr1_anti-CD28/anti-CD3	13.5	17.1
93573_Secondary Th1_resting day 4-6 in IL-2	0.0	0.0
93572_Secondary Th2_resting day 4-6 in IL-2	0.0	0.0

93571_Secondary Tr1 [illegible]ting day 4-6 in IL-2	0.0	0.0
93568_primary Th1_a[illegible]28/anti-CD3	0.0	0.0
93569_primary Th2_anti-CD28/anti-CD3	0.0	0.0
93570_primary Tr1_anti-CD28/anti-CD3	0.0	0.0
93565_primary Th1_resting dy 4-6 in IL-2	0.0	0.0
93566_primary Th2_resting dy 4-6 in IL-2	0.0	0.0
93567_primary Tr1_resting dy 4-6 in IL-2	0.0	0.0
93351_CD45RA CD4 lymphocyte_anti-CD28/anti-CD3	0.0	0.0
93352_CD45RO CD4 lymphocyte_anti-CD28/anti-CD3	0.0	0.0
93251_CD8 Lymphocytes_anti-CD28/anti-CD3	0.0	0.0
93353_chronic CD8 Lymphocytes 2ry_resting dy 4-6 in IL-2	0.0	0.0
93574_chronic CD8 Lymphocytes 2ry_activated CD3/CD28	0.0	0.0
93354_CD4_none	5.8	0.0
93252_Secondary Th1/Th2/Tr1_anti-CD95 CH11	0.0	0.0
93103_LAK cells_resting	0.0	0.0
93788_LAK cells_IL-2	0.0	0.0
93787_LAK cells_IL-2+IL-12	0.0	0.0
93789_LAK cells_IL-2+IFN gamma	0.0	0.0
93790_LAK cells_IL-2+ IL-18	0.0	0.0
93104_LAK cells_PMA/ionomycin and IL-18	0.0	0.0
93578_NK Cells IL-2_resting	0.0	0.0
93109_Mixed Lymphocyte Reaction_Two Way MLR	0.0	0.0
93110_Mixed Lymphocyte Reaction_Two Way MLR	0.0	0.0
93111_Mixed Lymphocyte Reaction_Two Way MLR	0.0	0.0
93112_Mononuclear Cells (PBMCs)_resting	0.0	0.0
93113_Mononuclear Cells (PBMCs)_PWM	0.0	0.0
93114_Mononuclear Cells (PBMCs)_PHA-L	0.0	0.0
93249_Ramos (B cell)_none	0.0	38.2
93250_Ramos (B cell)_ionomycin	0.0	0.0
93349_B lymphocytes_PWM	0.0	68.8
93350_B lymphoytes_CD40L and IL-4	31.0	0.0
92665_EOL-1 (Eosinophil)_dbcAMP differentiated	0.0	0.0
93248_EOL-1 (Eosinophil)_dbcAMP/PMAionomycin	0.0	0.0
93356_Dendritic Cells_none	0.0	0.0
93355_Dendritic Cells_LPS 100 ng/ml	0.0	0.0
93775_Dendritic Cells_anti-CD40	32.5	0.0
93774_Monocytes_resting	0.0	0.0
93776_Monocytes_LPS 50 ng/ml	0.0	0.0
93581_Macrophages_resting	0.0	0.0
93582_Macrophages_LPS 100 ng/ml	0.0	0.0
93098_HUVEC (Endothelial)_none	0.0	0.0
93099_HUVEC (Endothelial)_starved	11.3	0.0
93100_HUVEC (Endothelial)_IL-1b	0.0	14.6
93779_HUVEC (Endothelial)_IFN gamma	0.0	0.0
93102_HUVEC (Endothelial)_TNF alpha + IFN gamma	0.0	0.0
93101_HUVEC (Endothelial)_TNF alpha + IL4	0.0	0.0
93781_HUVEC (Endothelial)_IL-11	0.0	0.0
93583_Lung Microvascular Endothelial Cells_none	0.0	0.0
93584_Lung Microvascular Endothelial Cells_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.0	0.0
92662_Microvascular Dermal endothelium_none	0.0	0.0
92663_Microsvasular Dermal endothelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.0	0.0
93773_Bronchial epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml) **	0.0	0.0
93347_Small Airway Epithelium_none	0.0	0.0
93348_Small Airway Epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.0	0.0
92668_Coronery Artery SMC_resting	0.0	0.0
92669_Coronery Artery SMC_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.0	0.0
93107_astrocytes_resting	0.0	0.0

93108_astrocytes_TNF[redacted]4 ng/ml) and IL1b (1 ng/ml)	0.0	0.0
92666_KU-812 (Basop[redacted]esting	0.0	40.3
92667_KU-812 (Basophil)_PMA/ionoycin	0.0	0.0
93579_CCD1106 (Keratinocytes)_none	0.0	0.0
93580_CCD1106 (Keratinocytes)_TNFa and IFNg **	0.0	0.0
93791_Liver Cirrhosis	100.0	99.3
93792_Lupus Kidney	0.0	0.0
93577_NCI-H292	0.0	0.0
93358_NCI-H292_IL-4	0.0	0.0
93360_NCI-H292_IL-9	10.6	0.0
93359_NCI-H292_IL-13	0.0	65.5
93357_NCI-H292_IFN gamma	0.0	24.8
93777_HPAEC_-	0.0	0.0
93778_HPAEC_IL-1 beta/TNA alpha	0.0	0.0
93254_Normal Human Lung Fibroblast_none	0.0	0.0
93253_Normal Human Lung Fibroblast_TNFa (4 ng/ml) and IL-1b (1 ng/ml)	0.0	0.0
93257_Normal Human Lung Fibroblast_IL-4	0.0	0.0
93256_Normal Human Lung Fibroblast_IL-9	0.0	0.0
93255_Normal Human Lung Fibroblast_IL-13	0.0	0.0
93258_Normal Human Lung Fibroblast_IFN gamma	0.0	0.0
93106_Dermal Fibroblasts CCD1070_resting	0.0	0.0
93361_Dermal Fibroblasts CCD1070_TNF alpha 4 ng/ml	0.0	43.8
93105_Dermal Fibroblasts CCD1070_IL-1 beta 1 ng/ml	0.0	0.0
93772_dermal fibroblast_IFN gamma	42.0	27.7
93771_dermal fibroblast_IL-4	10.7	90.1
93259_IBD Colitis 1**	0.0	0.0
93260_IBD Colitis 2	13.8	0.0
93261_IBD Crohns	0.0	46.7
735010_Colon_normal	15.6	0.0
735019_Lung_none	12.9	16.8
64028-1_Thymus_none	69.3	100.0
64030-1_Kidney_none	0.0	0.0

Taqman results in Table 18 demonstrate that clone FCTR6 is differentially expressed in clear cell Renal cell carcinoma tissues versus the normal adjacent kidney tissues and thus could have a potential role in the treatment of renal cell carcinoma.

EQUIVALENTS

Although particular embodiments have been disclosed herein in detail, this has been done by way of example for purposes of illustration only, and is not intended to be limiting with respect to the scope of the appended claims which follow. In particular, it is contemplated by the inventors that various substitutions, alterations, and modifications may be made to the invention without departing from the spirit and scope of the invention as defined by the claims. The choice of nucleic acid starting material, clone of interest, or library type is believed to be a matter of routine for a person of ordinary skill in the art with knowledge of the embodiments described

herein. Other aspects, advantages, and modifications considered to be within the scope of the following claims.